IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 11, Issue 2 Ver. II (Mar.- Apr.2016), PP 69-73
www.iosrjournals.org

Coenzyme Q10 Effect on Varicocele Associated Asthenozoospermia

Huda I. Al-Qadhi [1] ,Haidar M.Jawad [2], Usama S.Al-Nasiri [3]
[1]*lecturer/College of medicine/Department of Pharmacology/University of Baghdad. Baghdad. Iraq*
[2]*assistant professor/college of Medicine /Department of Pharmacology. University of Baghdad. Baghdad. Iraq*
[3]*Professor/ The Iraqi Board for Medical Specializations. Baghdad. Iraq*

Abstract
Back Ground: *Varicocele It Is One Of The Leading Causes Of Male Infertility. Although 15% Of Adult Men Are Believed To Have Either Clinical Or Subclinical Varicocele, Its Prevalence May Be As High As 40% Among Infertile Men.*
Subfertile Men With Varicocele Have Disrupted Spermatogenesis, Which Is Manifested By Low Sperm Count, Decreased Sperm Motility, And A Low Percentage Of Normal Sperm Morphology.
By Providing Readily Available Energy For Use By Spermatozoa Thus Positively Affecting Sperm Motility, Maturation And The Spermatogenic Process, A Key Role In Sperm Metabolism Is Strongly Suggested By The High Levels Of Coenzyme Q10 In Epididymal Lumen And Sperm Cells.
Objective*: Placebo-Controlled, Double-Blind Randomized Trial Assigned To Determine The Efficacy Of Coenzyme Q10 Supplementation On Sperm Motility In Varicocele Patients .*
Patients And Methods: *A Total Of 52 Infertile Men With Varicocele Associated Asthenozoospermia (Progressive Motile Sperm ≤ 32% Within 60 Minutes) (WHO 2010) Were Randomly Assigned To Receive 200 Mg Coenzyme Q10 (Naturs Bounty, ING-USA) Orally Daily (27 In Group 1) Or A Similar Placebo Regimen (25 In Group 2) During A 6 Months Period. Monthly Follow Up By Semen Analysis Was Done.*
Main Outcome Measure*: Variations In Sperm Kinetic Parameters Used For Patient Selection*
Results*: Spermatozoa Motility Increased Significantly After Treatment, From 8.08±0.27 To 40.56±4.49 P= <0.001.*
Conclusion*: The Exogenous Administration Of Coenzyme Q10 Is Effective In Improving Sperm Kinetic Features In Patients Affected By Varicocele Asthenozoospermia.*
Keywords*: Male Infertility, Coenzyme Q10 Therapy, Varicocele Asthenozoospermia*

I. Introduction

The exact mechanism of impaired testicular function in patients with varicocele is not known. The most widely accepted concept is currently a varicocele related increase of testicular temperature. Normally, the difference between the intraabdominal and scrotal temperature averages 2.2ºC. Varicocele can cause an increase in scrotal temperature by 2.6ºC, neutralizing the required temperature gradient. However, there is considerable overlap between the range of scrotal temperatures in infertile men with varicoceles and in normal fertile men. The varicocele-associated pathology mainly includes changes in testicular size, histology, impaired leydig cell function (steroidogenesis), and sperm characteristics[1].

Excessive generation of reactive oxygen species (ROS) with inadequate compensatory rise in anti-oxidants is called oxidative stress. Oxidative stress may also be generated by deficiency of anti-oxidants without a change in the ROS levels . Oxidative stress found in the tubula and the seminal plasma of the majority of oligoasthenozoospermia(OAT) .ROS are mainly produced by leukocytes and immature gametes; therefore an increase in one or both cell types increases ROS and reduces TAC (total antioxidant capacity) . Varicocele has been associated with increased oxidative stress, especially in the gonads. Alterations in the testicular hemodynamics and microenvironment due to varicocele probably increases ROS production in association with decreased TAC.[2]

In OAT (oligoasthenoteratozoospermia),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. OAT 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) [3].

CoQ10 or ubiquinone, an isoprenylated benzoquinone that transports electrons from complexes I and II to complex III in the mitochondrial respiratory chain, is essential for the stability of complex III [4,5]. In addition, CoQ10 is an antioxidant, an energy promoting agent, a membrane stabilizer and a regulator of

mitochondrial permeability transition pores [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 varicocele asthenozoospermia 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.

Patients were classified as varicocele associated OAT (VOAT),clinical signs and scrotal echo color Doppler scanning findings of unilateral subclinical varicocele show a mean vien diameter (MVD)≤2.5 mm without reverse flow on valsalva's maneuvers. Patients with bilateral varicocele found with echocolor Doppler scanning are also included.

varicocele with clinical grade II or grade III, are excluded.

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.

Seminal Fluid Analysis: was done monthly

Sperm Motility And Grading: In recent years, a number of techniques for objective assessment of movement characteristics of human spermatozoa have been introduced by using computer-assisted semen analysis (CASA) systems. For the purpose of conventional analysis, a simple classification system which provides the best possible assessment of sperm motility without resorting to complex equipment is recommended. Motility was determined both quantitatively and qualitatively. For quantitative determination of sperm motility, a fixed volume of semen (not more than 10 µL) is delivered onto a clean glass slide and covered with a 22x22 mm coverslip. It is important that the volume of semen and the dimensions of the coverslip are standardized so that the analyses are always carried out in a preparation with fixed depth (i.e., 20 µm). This depth allows full expression of the rotating movement of normal spermatozoa. The preparation is then examined at a magnification of X400. An ordinary light microscope was used. The weight of the coverslip spreads the sample for optimal viewing. The freshly made, wet preparation is left to stabilize for approximately one minute. Motility estimation can conveniently be carried out at a room temperature between 18 and 24°c.

Qualitative sperm motility determined subjectively by grading the motility according to the standards of WHO, 2010. The microscopic field is scanned systematically and the motility of each spermatozoon encountered is graded according to what it shows:

(a) progressive motility.
(b) non-progressive motility
(c) Immotility.

Spermatozoa graded (a) are supposed to display rapid progressive motility along a linear track, covering a distance of ≥25 µm (half the length of a spermatozoon) per second [10]. At least 100 spermatozoa are classified in this way. Visual field close to the border of the coverslip should be avoided. This can be measured by the aid of ocular micrometer.

Tatistical Analysis

$$\text{Sperm motility percent} = \frac{\text{Number of motile sperm in 10 microscopic fields}}{\text{Total number of sperms in 10 fields}} \times 100$$

study, it was seen that 27 of the patients included in the CoQ10-treated group and 25 of the patients included in the placebo group completed the study.

The laboratory baseline data of sperm motility of all patients included in the clinical study are depicted in tables [1]. All patients had decrease in sperm motility below the normal readings of WHO 2010. (i.e. Asthenozoospermia)

There was no significant difference in semen parameters regarding motility, between data of baseline and values obtained after 6months of patients with asthenozoospermia receiving placebo.(table 2)While Patients undergoing Co enzyme Q10 therapy showed significant improvement in these semen parameters as the data of baseline was compared with the data after 6 months of treatment, from 8.08±0.27 to 40.56±4.49.(table 3).(figure1)

Table (1): Baseline data of sperm motility of all patients included in the clinical study. Values are means ± S.D (n = 25 placebo groups; 27 treatment groups).

Parameters	normal standard values	placebo	treatment
Progressive motile Sperms	>32% within 60minutes	17.07±0.26	18.08±0.27
Non progressive motile sperm		26.78±9.93	23.00±13.07
Immotile sperm		57.15±17.17	59.92±13.16

Table (2): Statistical analysis of changes on sperm motility of patients with asthenozoospermia receiving placebo after 6 months as compared to the baseline values. (n= 25 patients).

(Placebo)	Base Line	after 6 months
Progressive motile sperms	17.07±0.26	16.07±0.26
Non progressive motile sperms	26.78±9.93	25.00±8.17
Immotile sperms	57.14±17.17	59.14±13.58

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

Parameters	normal standard values	baseline	after 6 months
Progressive motile Sperms	>32% within 60minutes	8.08±0.27	40.56±4.49
Non progressive motile sperm		23.00±13.07	37.00±26.12
Immotile sperm		59.92±11.75	23.44±11.21

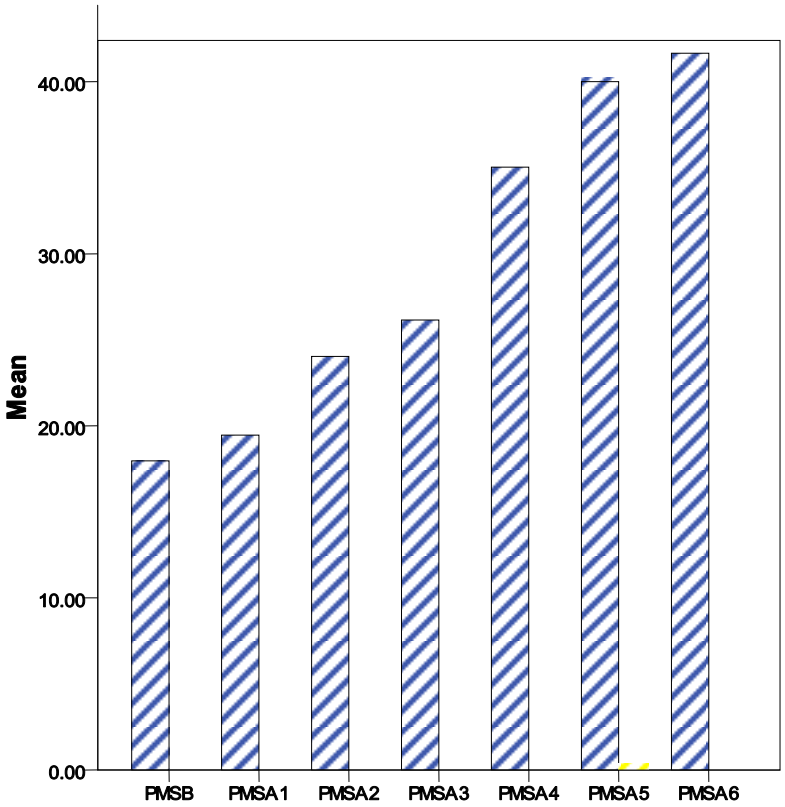

Figure (1): <u>Progressive motile sperms (PMS)</u> of patients at baseline(B) and throughout the 6 months course of treatment with CoQ10 (A1 to A6). P<0.005

IV. Discussion

In varicocele the role of ROS has also been extensively investigated. Varicocele has been associated with increased oxidative stress, especially in the gonads [11]. Alterations in the testicular hemodynamics and microenvironment due to varicocele probably increase ROS production in association with decreased seminal plasma and blood antioxidant defenses in the infertile varicocele patients when compared with the controls [12].

Excessive ROS levels are related to an increase in lipid peroxidation of the sperm plasma membrane leading to motility and morphology alterations and even to cell death [13-15].Lipid peroxidation results in loss of membrane fluidity, which is essential for sperm motility and sperm-oocyte fusion [16-18]. Motility is impaired either because of adenosine triphosphate depletion in axons or lipid peroxidation of the sperm plasma membrane [19]. Spermatids and mature spermatozoa are deemed highly sensitive to ROS because their membranes are particularly rich in polyunsaturated fatty acids (PUFA) [20].

The potentially damaging effects of ROS in sperm cells and seminal plasma are counteracted by protective antioxidant systems. The enzymatic defence systems such as catalase, superoxide dismutase (SOD), and glutathione peroxidase are lower in spermatzoa than in seminal plasma which is rich with antioxidant buffer capacity [21]. A low concentration of scavenging enzymes make the PUFA highly susceptible to peroxidation by elevated levels of ROS, so the protection of membranes from oxidative stress (OS) is essential for preserving sperm integrity and membrane fluidity [22]. There is correlation between leukocyte concentrations, ROS levels, lipid peroxidation, and functional damage [23]. The location of CoQ_{10} in membranes in close proximity to the unsaturated lipid chains allows it to act as a primary scavenger of free radicals. CoQ_{10} amount in many membranes is from 3 to 30 times the tocopherol content [24]. The quinol form of CoQ_{10} in cell membranes makes it very effective antioxidant [25]. CoQ_{10} have essential role in regeneration of tocopherol by reaction with lipid or oxygen radicals so rescue tocopheryl radicals [26].

V. Conclusions

The conclusions which can be drawn from the present study are that CoQ_{10} clinically lead to improvement of sperm motility and provide good non hormonal treatment for patients with history of infertility.

Author Contribution

study conception: Dr.Haidar Mahdi and Dr.Usama Alnasiri.
Study desgn: Dr.Haidar Mahdi ,Dr.Usama Alnasiri and Dr.Huda Ibraheem.

Data acquisition and interpretation: Dr.Huda Ibraheem
Drafting of manuscript and critical revision: Dr. Huda Ibraheem

References

[1]. Word Health Organization, (1992): WHO Laboratory Manual For Examination Of Human Semen And Semen Cervical Mucus Interaction. 3rd Edition Cambridge University Press Cambridge.
[2]. World Health Organisation, (1992): The Influence Of Varicocele On Parameters Of Fertility In A Large Group Of Men Presenting To Infertility Clinics. Fertil Steril; 57:1289-93.
[3]. Giorgio Cavallini, (2006): Male Idiopathic Oligoasthenoteratozoospermia. Asian J Androl ;Mar; 8: 143–157
[4]. Baker HWG, Burger HG, De Krester DM, Hudson B., (1986): Relative Incidence Of Etiological Disorders For Male Infertility, In: R.J. Santen, R.S. Swerdloff (Eds.), Male Reproductive Dysfunction, Marcel Dekker, New York, P. 350
[5]. Aitken RJ, Krausz C. Oxidative Stress, DNA Damage And The Y Chromosomreproduction 2001;122:497–506
[6]. Groneberg D, Kindermann B, Althammer M, Klapper M, Vormann J,Littarru GP, Et Al. Coenzyme Q10 Affects Expression Of Genes Involved In Cell Signalling, Metabolism And Transport In Human Caco-2 Cells. Int J Biochem Cell Biol 2005;37:1208–18.
[7]. Mancini A, De Marinis L, Oradei A, Hallgass E, Conte G, Pozza D, Et Al. Coenzyme Q10 Concentration In Normal And Pathological Human Seminal Fluidj Androl 1994;15:591–4.
[8]. Balercia G, Arnaldi G, Fazioli F, Serresi M, Alleva R, Mancini A, Et Al. Coenzyme Q10 Levels In Idiopathic And Varicocele-Associated Asthenozoospermia.
[9]. Andrologia 2002;34:107–11.
[10]. 9- Mancini A, De Marinis L, Littarru GP, Balercia G. An Update Of Coenzyme Q10 Implications In Male Infertility: Biochemical And Therapeutic
[11]. Aspects. Biofactors 2005;25:165–74.
[12]. Comhaire FH, Cristophe AB, Zalata AA, Dhooge WS, Mahmoud AM, Depuidt CE., (2000): The Effects Of Combined Conventional Treatment, Oral Antioxidants And Essential Fatty Acids On Sperm Biology In Subfertile Men. Prostaglandins Leukot Essent Fatty Acids.; 6:159–165.
[13]. 11-Aitken RJ, Buckingham D, And Harkiss D (1993): Use Of A Xanthine Oxidase Free Radical Generating System To Investigate The Cytotoxic Effects Of Reactive Oxygen Species On Human Spermatozoa, J Reprod Fertil., 97, 441–450.
[14]. 12- Saleh R A, Agarwal A, Sharma R K, Said T M, Sikka S C, Thomas Jr S C, (2003) "Evaluation Of Nuclear DNA Damage In Spermatozoa From Infertile Men With Varicocele", Fertil Steril;80;(6): Pp. 1,431–1,436..
[15]. 13- Agarwal, Said (2003): Role Of Sperm Chromatin Abnormalities And DNA Damage In Male Infertility, Hum Reprod Update, 9, (4), 331–345.
[16]. 14- Dorota S. And Maciej K., (2004): Reactive Oxygen Species And Sperm Cells. Reprod Biol Endocrinol.; 2: 12.
[17]. 15- Fingerova H, Oborna I, Novotny J, Svobodova M, Brezinova J, Radova L., (2009): The Measurement Of Reactive Oxygen Species In Human Neat Semen And In Suspended Spermatozoa: A Comparison. Reprod Biol Endocrinol. 27; 7:118.
[18]. 16- De Lamirande E, And Gagnon C, (1992): Reactive Oxygen Species And Human Spermatozoa. II. Depletion Of Adenosine Triphosphate Plays An Important Role In The Inhibition Of Sperm Motility. J Androl 13: 379–386.
[19]. 17- Koppers AJ, Garg ML, Aitken RJ., (2010): Stimulation Of Mitochondrial Reactive Oxygen Species Production By Unesterified, Unsaturated Fatty Acids In Defective Human Spermatozoa. Free Radic Biol Med. 1; 48(1):112-9.
[20]. 18- Smith R, Vantman D, Ponce J, Escobar J, And Lissi E. (1996) Total Antioxidant Capacity Of Human Seminal Plasma. Hum. Reprod. 11, 1655 – 1660
[21]. 19- Jones, R., Mann, T., And Sherina, R. (1979) Peroxidative Breakdown Of Phospholipids In Human Spermatozoa, Spermicidal Properties Of Fatty Acid Peroxides, And Protective Action Of Seminal Plasma. Fertil. Steril. 31, 531 – 537.
[22]. 20- Ford, W.C.L. And K. Whittington, (1998). Antioxidant Treatment For Male Subfertility: A Promise That Remains Unfulfilled. Hum. Reprod., 13: 1416-1419.
[23]. 21- Turunen M, Sindelar P, Dallner G (1999): Induction Of Endogenous Coenzyme Q Biosynthesis By Administration Of Peroxisomal Inducers.Biofactors 9:131–140.