ORIGINAL ARTICLE

Role of Coenzyme Q10 Supplementation on Semen Parameters in Infertile Men: A Quasi Experimental Study

FAWAD NASURULLAH , SHAMS-UL-ISLAM, KAMRAN ZAIDI*, *MUHAMMAD WAQAS HUSSAIN, MUHAMMAD HAIDER*
Department of Urology, Mayo Hospital, Lahore
**Assistant Professor Urology, PGMI, Lahore*
Correspondence to Dr. Shams ul Islam, Assistant Professor Email: dshamsulislam@gmail.

ABSTRACT

Aim: To determine the effect of coenzyme Q10 on improvement of total sperm count and sperm motility in infertile men.
Study Design: Quasi experimental Pilot study
Settings: Urology ward, Mayo Hospital Lahore
Methods: Twenty nine married male patients aged 18-40 years who had failure to cause pregnancy after 12 months or more of unprotected sexual intercourse with oligoasthenospermia and normal blood serum FSH, LH, and total testosterone and normal external genitalia were included and randomly divided into Treatment group and Placebo group. Cases were given 200 mg CoQ10 once daily for 3 months and group B were given placebo (Ferrous sulphate 200mg).Semen analysis was done at baseline and then after 3 months of treatment.
Results: Twenty nine patients meeting the inclusion criteria were included in this pilot study after written consent. All of these cases were married and had BMI <30 (non-obese). Age ranged from 20 to 33 years with total sperm count ($x10^6$) at baseline was 30.8± 26.7 and after 3 months of treatments was 72.3±38.4 while sperm motility at baseline was 29.6±18.6 and after 3 months of treatment was 50 ± 26 in the treatment group. The significant improvement in the sperm count and motility (≥50% increase) in the treatment group noted in this pilot study was 85.7% and 78.6%.
Conclusion: In our pilot study, sperm count and sperm motility significantly improved after 3 months treatment with CoQ10. Further conclusions can be made when the trial will be complete. This study should be extended further to follow patients till a successful pregnancy and/or live birth.
Keywords: Coenzyme Q, Infertility, Subfertility, Oligospermia, Trial, Pilot study, Urology, Sperm count, Motility

INTRODUCTION

Infertility affects an estimated 15% of couples globally, amounting to 48.5 million couples .Males were found to be solely responsible for 20-30% of infertility cases and contribute to 50% of cases overall[1]. Another study reported that it affects 7% of all men. It is commonly due to deficiencies in the semen, and semen quality is used as measure of male fecundity[2].

Male infertility is becoming a real health problem which has increased over the last decades.[3,4] Several recent studies have suggested that sperm concentrations and semen quality have been decreasing over the past several decades in many areas of the world. Acute events can have significant impacts on spermatogenesis and are often readily identified during the male fertility evaluation. The majority of male factor infertility, however, is idiopathic.[5] The main causes of male infertility are testicular insufficiency due to congenital and acquired causes, obstructions of the male genital tract, genetic and endocrine abnormalities, urogenital infections and varicocele.[6] Other possible factors may be associated with sub fertility include obesity, tobacco use, and excessive alcohol intake[7].

Nutritional supplements, herbal medications, acupuncture, mind-body practice, scrotal cooling, and faith-based treatments were increasingly utilized in addition to, or instead of, conventional allopathic approaches[7] Moreover, modern medicine has made several advances in the diagnosis, treatment and prevention of infertility. However, most infertile men with idiopathic oligoasthenoteratospermia have remained untreated. Treatment for idiopathic male infertility is empirical.[8] Both the bioenergetic and the antioxidant role of CoQ10 suggest a possible involvement in sperm biochemistry and male infertility as well.

CoQ10 can be quantified in seminal fluid, where its concentration correlates with sperm count and motility[11,12]. The current study was planned to see the effect of coenzyme Q10 on improvement of total sperm count and sperm motility in infertile men of Pakistani population. As no local data is available and male infertility has now become very common compliant in our OPDs, Q10 may be effective for improving sperm count and motility, and resolving subfertility from our population.

Received on 23-01-2020
Accepted on 13-06-2020

MATERIALS AND METHODS

The quasi experimental pilot study was conducted in Department of urology, Mayo Hospital Lahore after approval from ethical review committee. 29 married male patients aged 18-40 years who had failure to cause pregnancy after 12 months or more of unprotected sexual intercourse with oligoasthenospermia and normal blood serum FSH, LH, and total testosterone and normal interpretation of ultrasound of external genitalia were included in the study and randomly divided into Treatment group (Group A) and Placebo group (Group B). Male infertility was defined as inability to cause pregnancy in a fertile female after 12 months or more of regular unprotected sexual intercourse. If after 3 months of trial there was 50% or more increase in total sperm count and percentage of active, motile sperms from the baseline, it was labeled as successful improvement. Normal sperm densities range from 15 million to greater than 200 million sperm per mililiter of semen. All those patients diagnosed with azoospermia, previously had vasectomy, or were having scrotal pain due to varicocele, inguinal hernia, spermatocele assessed clinically, with history of epididymoorchitis, testicular torsion, prostatitis, genital trauma, inguinal or genital surgery and those who were on cytotoxic drugs, immunosuppressant, anti-convulsive, anti-androgens or had recent history of sexually transmitted disease were excluded from the study.

A written informed consent was taken from each participant after explaining the complete details of the study. After taking a complete medical and reproductive history i.e. exploring all aspects that may be related to fertility, all patients were examined physically and urinalysis with serum chemical analysis for serum FSH, LH, and total testosterone levels, semen samples, and hematological laboratory tests were sent.

All patients were asked to complete a face-to-face questionnaire, regarding occupational history and lifestyle. A baseline semen analyses was done. Semen samples were obtained in a sterile wide mouth and metal-free plastic container after 3 days of recommended sexual abstinence. All cases in this pilot study were given 200 mg CoQ10 once daily for 3 months. All patients in the in the group B were given placebo drug which is decided as Tab Ferrous sulphate 200mg.Compliance was assessed by comparing the number of pills ingested with the number of days between dispensing visits. Follow-up appointments were done and at the end of 3rd month and semen samples were collected for analysis of sperm count and motility. Complete data was collected by the researcher himself (Dr. Sham-ul-Islam).

All the data was entered and analyzed through SPSS version 22. Mean ± standard deviation was calculated for all quantitative variables like age, sperm count at baseline, after 3 months, rise in sperm count, sperm motility at baseline, after 3 months and rise in sperm motility. Frequency and percentages were calculated for all qualitative variables like successful improvement in sperm count and motility (as per operational definition), obesity, marital status and BMI. Data was stratified over age, marital status and BMI (obese/non-obese) to address effect modifiers. Post stratificationchi-square test was applied and p-value ≤ 0.05 was taken significant.

RESULTS

In this pilot study, 29 patients initially meeting the inclusion criteria were included after written consent. All of these cases were married and had BMI <30 (non-obese). 14 were randomly taken in group A (intervention group/cases) and 15 in the group B (placebo group/controls). Age of the patients in group A ranged from 20 to 33 years with mean±SD 28.1±4 years. On semen analysis at the start of the trial, total sperm count was 30.8±26.7 million/ml of the semen and percent motility of sperms was 29.6±18.6. (Table 1) Compliance of the patients was more than 90% in all the patients. Age of group B ranged from 22-38 with mean±SD 30.1±4 years. On semen analysis at the start of the trial, total sperm count was 23.7±8 million/ml of the semen and percent motility of sperms was 26.5±11.4. (Table 1)

After 3 months of trial of Q10, semen analysis of patient in group A showed total sperm count of 72.3±38.4 million/ml versus 25.1±9.0 in the group B and percent motility of sperms was 50±26.1vs26.5±11.4 in the group B.Total sperm count increased after 3 months of trial by 41.5±27 in group A vs4.1 ± 4.0 in group B (p-value <0.001)and rise in motility of sperms by 21.8±14.9 in group A vs4.7±5 in group B (p-value <0.001). (Table: 2)

Percentage rise in the total sperm count in the group A was 140% and percent rise in motility of the sperms was 72%. All patients had a very high percentage of slow/sluggish sperms at the start of the trial. Percentage of slow/sluggish sperms in group A was 70.4±18.6 at the start of the trial and after 3 months of Q10 treatment the percentage of slow/sluggish sperms became 49.3±27.2, with a percent fall of 32%.

The significant improvement in the sperm count and motility (≥ 50% increase) noted in this pilot study was 85.7% and 78.6% of the patients in group A.

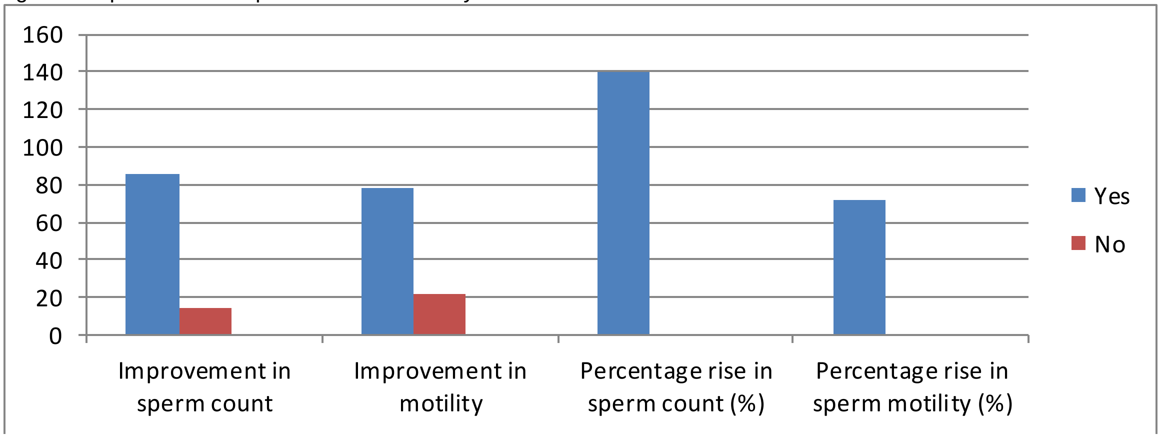
Table 1: Baseline characteristics at baseline before trial

Characteristics	Treatment Group A-	Placebo Group B
Age: Mean±SD (min-max)	28.2±4 years (20-33)	30.1±4 years (22-38)
Sperm count: Mean±SD (min-max)	30.8 ± 26.7 million (5-110)	23.7± 8 million (11-36)
Sperm Motility (%): Mean±SD (min-max)	29.6 ±18.6 (4-60)	26.5± 11.4 (8-46)
Slow/Sluggish Sperms: (%) Mean±SD (min-max)	70.4 ±18.6 (46-96)	39.2± 13.9 (22-63)
BMI<30: ≥30	100% (n=14) 0% (n=0)	100% (n=15) 0% (n=0)
Obesity Yes No	100% (n=14) 0% (n=0)	100% (n=14) 0% (n=0)

Table2: Improvement in sperm count and motility after 3 months of Q10 trial

Characteristics	Cases	Difference from baseline	Placebo group	Difference from baseline
Sperm count: Mean±SD (min-max)	72.3± 38.5 (10 -120)	41.5± 27.0 (2-80)	25.1± 9.0 (10-40)	4.1 ± 4.0 (0-12)
Sperm Motility (%) Mean±SD (min-max)	50 ±26.2 (10-80)	21.8±14.9 (9-49)	28.8±10.9 (9-49)	4.7± 5 (0-14)
Slow/Sluggish Sperms (%) Mean ± SD (min-max)	49.3± 27.2 (10-90)	22.5±16 (0-50)	39.3±13.8 (15-64)	39.3±13.8 (0-10)

Figure 1: Improvement in sperm count and motility after 3 months of trial in cases



DISCUSSION

With advancements in modern medicine, diagnosis, management and prevention of infertility among males have been revolutionized. Still males with idiopathic oligoasthenoterato-spermiaare looking for treatment.[8] Beneficial effects of zinc, selenium, vitamin C, CoQ10, d-aspartate and other anti-oxidants are under trials for the management of subfertility. Excess ROS (reactive oxygen species)damages the cell membranes and disturbs the sperm cell function [8] and antioxidants including CoQ10 or ubiquinone with its bioenergeticproperty as a proton and electron carrier in the mitochondria membrane and as ubiquitous in other biological membranes improves sperm cell function and their survival.[9,10]CoQ10is alipid-soluble entity involved in electron transport chain and production of ATP. It act as an antioxidant itself and also support regeneration of various other anti-oxidants, thus promoting growth and protecting the cell[13].

The role of CoQ10in cardiovascular physiology is proven, even as an independent predictor of mortality. Its role has also been studied on gene induction mechanisms, Parkinson's, Huntington's diseases and Friedreich's ataxia. Trials have showed a decrease in the incidence of preeclampsia and headache symptoms in adults, paediatric and adolescents[14]. Groneberg DA, et al concluded that CoQ10 causes an increased expression of 694 genes at threshold-factor of 2.0 or more. Only one gene was down-regulated 1.5-2-fold. Real-time RT-PCR confirmed the differential expression for seven selected target genes[15]. Littarru GP, et al induced that dietary supplementation with CoQ10 results in increased resistance of low-density lipoproteins to the initiation of lipid peroxidation. And have a direct effect on endothelial function. Also shown to improve cardiac contractility, seminal fluid integrity and sperm cell motility[16].

Similar to our study results, Safarinejad MR, et al reported baseline total sperm count (x10^6) 46.6 ±12.6 and after 26 weeks of treatments 57.6 ± 14.4 with sperm motility at baseline to be 22.2 ± 2.4% and of 26th weeks of treatment was 27.6 ± 2.2[8]. But, Nadjarzadeh A, et al reported oppositely; concluded that CoQ10 treatment had non-significant changes on the semen parameters although total antioxidant capacity of seminal plasma significantly improved ($p<0.05$), but effects on sperm concentration, motility and morphology were non-significant; CoQ10 can be used as adjunct and further studies are required[14].

Even in the patients with varicocele, having a higher level of oxidative stress, distribution of CoQ10 between sperm cells and seminal plasma was altered. Mancini A, et al reported that CoQ10trial showed positive results with improvement in the sperm function but still more work should be done[11]. Barbato V, et al and Al Mosavi,et al reported a lot of work on the adverse effects of ROS on fertility like disturbance of sperm motility, DNA fragmentation, and reduction of chances of fertilization; but zinc, d-aspartate and co-enzyme Q10prevent these changes[20]. Balercia G, et al trial reported increase in CoQ10 and ubiquinol significantly in both seminal plasma and sperm cells after treatment leading to increase in spermatozoa motility[13,21]. Balercia G, et al reportedafterCoQ10 and ubiquinol trials on 82 patients also reported the same results and concluded that those with lower baseline motility and CoQ10 levels responded more to the treatment[22]. These results were consistent with our results.

In a randomized clinical trial with longer follow-up to know the pregnancy rate and birth rate, Lafuente R, et al. studiedCoQ10 seminal concentration, sperm concentration, and sperm motility and reported that no evidence in the literature was found previously regarding live birth or pregnancy rates after CoQ10 trial[17]. Showell MG, et al reported after a meta-analysis of 34 trials on 2876 couples following them for live births, that about 96 pregnancies occurred in 964 couples after trial and 20 live births occurred in 214 couples ($P < 0.00001$); with no evidence of any side effects[23].

In another meta-analysis, Showell MG, et al reported 48 randomized clinical trials of antioxidants treatment in 4179 sub-fertile menbut only three showed live birth or clinical pregnancy. Chance of a live birth after CoQ10 trial is between 10% - 31% versus 5% after placebo or no treatment. Chance of clinical pregnancy afterCoQ10 increased the chance of clinical pregnancy following treatment from 6% to 28%.A chance of miscarriage in these pregnancies was reported to be very low but it still only three trials have been done in this regard[24].

Young SS, et al reported that men with high folate intake (>75th percentile) and with high antioxidants intake had fewer frequencies of disomies, sex nullisom and lower sperm aneuploidy (P <or= 0.04)[19].

Similar to our study, Safarinejad MR, et al revealed significant improvement in sperm density and motility (each p = 0.01) and increase in normal forms of sperms in the coenzyme Q10 group (p = 0.07). They also concluded that longer treatment duration with CoQ10 showed better improvement in sperm count (a positive correlation, p = 0.03); same was also seen with sperm motility (p = 0.04) and sperm morphology (p = 0.04). The acrosome reaction also increased from 14% to 31% in the coenzyme Q10 and placebo groups, respectively (p = 0.01)[25].

Similar to previous studies quoted, antioxidants including zinc and CoQ10 showed significant improvement in the sperm count and sperm motility. As the trial is still not complete no conclusion can be made. We need longer follow-up of these patients to draw any final conclusion and to evaluate the positive and negative effects of CoQ10 supplementation in sub-fertile men on birth rate and pregnancy rate.

CONCLUSION

No previous trial has been done on the effects of antioxidants like CoQ10 in our region. In our pilot study, sperm count and sperm motility significantly improved after 3 months treatment with CoQ10. Further conclusions can be made when the trial will be complete. This study should be extended further to follow patients till a successful pregnancy and/or live birth.

Conflict of interest: All the authors declared no conflict of interest.

Limitation of the study: This is a pilot study and study is going on and still incomplete. We cannot estimate the level of antioxidants in the semen, detailed morphology of the sperms and any changes up to chromosomal /DNA level can also not been checked due to limited resources and expensive natures of tests.

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