RESEARCH ARTICLE

Using of the L-Arginine and Co-Enzyme Q10 Shows Improvement of the Male Subfertility

Mazin A Hasoon

Surgery Department, College of Medicine, University of Thi-Qar, University in Nasiriyah, Iraq.

Received: 17th Oct, 19; Revised: 13th Nov, 19, Accepted: 15th Dec, 19; Available Online: 25th Dec, 2019

ABSTRACT

Background: Infertility remains both prevalent and problematic among couples worldwide, where abnormal semen quality or sexual dysfunction are contributing factors in about half of subfertile couples. Oxidative stress has been a well-studied etiology of abnormal semen parameters. Reduced fertilizing capacity is related to raised concentrations of reactive oxygen species in semen, which may damage the cell membrane. Multiple over-the-counter therapies have been historically used for male fertility like (Coenzyme- Q10, and Arginine).

Objectives of study: To determine the role of some of the antioxidants in the improvement of the semen parameters in a subfertile male, improvement by (coenzyme, q10 l-arginine) therapy.

Method: An experimental interventional non-randomized clinical trials study for exploring the male sub-fertility improvement by (L-arginine and Co-enzyme-Q10) therapies- in Al Nasiriyah City in 2019. Sample size The study contained three groups. Each group contains eight included responders. Male-patient responders who were diagnosed to have unexplained sub-fertility by a specialist gynecologist and urologist after excluding all organic causes of the subfertility, SPSS version 24 had been used for data analysis, paired t-test, correlation regression analysis had been used, where p-value < 0.005 considered as significant.

Result: A total of 24 patients with infertility, their mean age was 32 + –6.52 years, had been recruited within the study, with a very high significant statistical difference (p value < 0.005) between the first and the second occasions of measures and also between the first and the third occasions of measures, regarding volumes, counts, number of active sperms, number of active sperms, number of sluggish sperms, number of non-active sperms and number of abnormal sperms. By correlation regression analysis, there was a significant positive correlation of the independent parameters with the types of management modalities, where crossly examined by correlation regression. It was evident that all parameters except the counts are positively correlated by which p-value < 0.05.

Conclusion: This study concluded that the administration of Co-Enzyme, L- Arginine, and combination of both show improvement in most of the parameters of the semen. The combination was the first improver of the semen parameter followed by arginine, then the Co-Enzyme only, the volume, sperm morphology, and the activity were the main parameters affected by the multiple strategies of treatment protocols. Adding of the co-Enzyme to the protocol of the L-Arginine as a good semen volume incrementer, activity enhancer, abnormal morphology reducer.

Keywords: Al-Nasiriyah, Co-enzyme Q10, Iraq, L-Arginine, Subfertility.

International Journal of Drug Delivery Technology (2019); DOI: 10.25258/ijddt.9.4.6

How to cite this article: Hasoon, M.A. (2019). Using of the L-Arginine and Co-Enzyme Q10 Shows Improvement of the Male Subfertility. International Journal of Drug Delivery Technology, 9(4): 544-551.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Male subfertility refers to a male's inability to cause pregnancy in a fertile female, which is commonly due to deficiencies in the semen, and semen quality.[1] Infertility remains both prevalent and problematic among couples worldwide.[2] Abnormal semen quality or sexual dysfunction are contributing factors in about half of subfertilee couples.[3]

Oxidative stress has been a well-studied etiology of abnormal semen parameters. Reduced fertilizing capacity is related to raised concentrations of reactive oxygen species in semen, which may damage the cell membrane.[4] Multiple over-the-counter (OTC) therapies have been historically used for male fertility like (Coenzyme, Q10 Arginine).[5]

Coenzyme Q10 forms an integral part of cellular respiration and hence the production of energy. L-arginine plays a role in autocrine and paracrine regulation of spermatogenesis Semen analysis is the cornerstone of male fertility assessment.[6]

Male-subfertility is approximately 15% worldwide, 50% of infertility cases, sole reason in about 20% and contributory factor in 30–40% of the cases.[7] According to operation Iraqi

**Author for Correspondence: mtqr86@gamil.com*

freedom (OIF) about 13.8% of Iraqi men had experienced infertility.[8]

Risk factors are consisting of advanced age, stress, subfertility duration, genetic defects, chronic inflammatory and autoimmune diseases.[9]

Preventive measures are including maintenance of healthy lifestyle practices: smoking cessation and stop alcohol with regular exercise for an hour at least twice a weekly.[10]

Problem Statement

Reproduction is a natural and straightforward concern for most couples. Infertility, defined as "the inability to conceive after one year of unprotected intercourse".[11]

The (WHO) defines male factor infertility as the "presence of ≥1 abnormality in the semen analysis or the presence of inadequate sexual or ejaculatory function".[12] A man's fertility generally dependents on the quantity and quality of his sperms.[4]

Decrease fertilizing ability is related to elevated concentrations of reactive oxygen compounds in semen, which may destruct the cell membrane. [10]

Many antioxidant agents have been utilized in idiopathic male infertility. Coenzyme Q10 acts as an integral part of cell respiration and hence the creation of energy. L-Arginine plays a role in endocrine regulation of spermatogenesis.[13]

Rationale and Justification

In Iraq, childlessness social stigma still directs to neglect and isolation with negative psycho-social consequences in many developing countries as compared to developed societies.[14]

About 50% of sub-fertile couples presented with abnormal semen quality and sexual dysfunction. Sperm are rich in fatty acids which susceptible to oxidation, and as well-studied etiology, oxidative stress leads to abnormal semen parameters.[15]

From academic standpoint, it is essential to conduct an interventional analytical study to be a step in the way of answering the question of this problem.

Research Question

The general question of this study:

What is the effect of the OTC therapies (Co-enzyme Q10 and L-arginine) on semen quality and male subfertility improvement within the Iraqi environmental conditions?

This study is academic research to find an appropriate answer to this question.

Hypothesis suggestion

It is assumed that the semen quality improvement can be achieved by certain OTC administration (L-arginine and CoenzymeQ10) after excluding all organic etiology in sub-fertile male-patients.

Purpose of the study

This study is an attempt to find an accessible therapy for the socially and psychologically suffered sub-fertile males and couples.

It is a trial for enriching the local fertility centers modalities for treatment in unexplained or idiopathic males' infertility that it is hoped to be applied on the ground in the future.

Objectives of Study

General objective: Social problem solving for unexplained childlessness and eventually family sability in the Iraqi community

Specific objective: Showing the male subfertility improvement by (L-arginine and co-enzyme Q10) therapy.

METHODOLOGY

Profile of Study: Al-Nasiriya city

The study was conducted in Al-Nasiriyah city-the capital of Thi-Qar governorate- which is the 4th most populated city in Iraq.[16] It is located southeast of Baghdad on Euphrates River, about (370 km). According to the Central Statistic Organization of Iraq, there is about (2,040,126) calculated population in 2014.[17] Al Nasiriya city population appraised in 2017 (793472 individuals) by Thi-Qar Statistics Directorate with a male to female ratio 1:1.1 approxemaitly.[18]

Population of Study

Male-patient responders who were diagnosed to have unexplained sub-fertility by infertility specialist physician after excluding of all organic causes of the male subfertility. They included in the sample frame after obtaining their full consent for participating in the clinical trials study with an explanation about the administrating routes, side effects, duration, and pre-planned hoped results.

Exclusion Criteria

Those who were being inconsistent for consecutive follow-up within the study period and poor complained participants

Participants with organic or obstructive infertility.

Sample size:

Contained 24 included responders with a documented diagnosis.

Study design

An experimental interventional non -randomized clinical trial study for exploring the male sub-fertility improvement by (L-arginine and Coenzyme-Q10) therapies- in Al Nasiriya City in 2018.

The study contained three groups. Each group contains eight included responders.

First group: Received L-arginine (1000 mg) once time daily.
Second group: Received Coenzyme-Q10 (200 mg) once time daily.
Third group: Received a combination of the (L-arginine and Co-enzyme-Q10) (same doses above).

Follow up time -period of the study was 8 months with the monitoring seclude by seminal fluid analysis as 2 monthly for 4 months then after 4 months. i.e. (after 2 months, then after 2 months, then after 4 months).

Data Collecting and Analysis

Data has been gathered by a modified questionnaire of seminal fluid analysis formula according to WHO Criteria [19] with certain related demographic data. The data processed and analyzed by using the Statistical Package for Social Science (SPSS) version 25.[20] Descriptive Statistics and Inferential Statistics: Measures of Central Tendency and Results representation by graphs, tables.

Definition of Variables

Demographics are statistical data of the personal characteristics: age, gender and people income within the population.[21]
Name: A word or set of words by which a person is known, addressed, or referred to.[22]
Age: The duration that has elapsed since birth.[23]
Sex: Biologic and anatomical trait or quality that distinguishes male and female.[24]

Reference Limits of a Semen Analysis (WHO, 2010)[9,25]

Semen volume with reference value 1.5 mL (1.4–1.7).
PH: Measurement of acidity and alkalinity with normal value 7.2 or more.
Sperm concentration: No. of the sperm per ml of the seminal fluid (million/mL) with normal value ≥20 million/ml.
Total sperm count (millions per ejaculate) with normal range: 39 (33–46).
Total motility: sperm mobility (progressive + non-progressive) with normal limit equal to ≥ 50 % of the sperms.

Vitality (live spermatozoa %) which accounts about 58 % (55–63).

Tools and materials

Seminal fluid analysis

Laboratory test of sampled of seminal fluid, usually consisting of the recognizing of semen volume, semen (pH), count, shape, motility, and viability of sperm, which is done to test for possible male infertility.[26] The examination of fresh sperm should be done within 30 min. Before obtaining the sample, it has become traditional to demand ejaculation abstinence for 2–3 days.[27]

L-arginine

Essential amino acid and a key portion of proteins Lack of arginine in food decreases the sperm count and impairs child growth.[28] Arginine is available in turkey (bird), chicken, and bird meats, and as L-arginine in supplements.[29]

Co-enzyme Q10

Fat-soluble antioxidant and an important substance used in oxidative respiration for the Krebs cycle for the generation of energy for all body cells. It was first identified in 1957.[30] It presents in meats and seafood and can also be created in a laboratory and used for preventing Parkinson's disease, migraine, and many other conditions.[31]

RESULT

A total of 24 patients with infertility and mean age range 32+-6.52 years, had been recruited within the study, where they subcategorized into three main groups equally, (eight for each). The first group takes the co-enzyme, the second had been taken the L-arginin, the third group takes the combination of both, followed for at least six months, and checked at least three visits.

Table 1 showing very a high significant statistically difference (p value <0.005) between the first and second occasions of measures and also between the first and the third occasions of measures, regarding volumes, counts, number of active sperms, number of active sperms, number of sluggish sperms, number of non-active sperms and number of abnormal sperms.

Table 1: Distribution of the Patient's Parameters According to their three occasions of Sample Collections

			95% Confidence interval of the difference			
	Mean	*Std. deviation*	*Lower*	*Upper*	*t*	*Sig. (2-tailed)*
1st volume	3.0729	1.14084	2.5912	3.5547	13.196	
2nd volume	3.3542	1.24655	2.8278	3.8805	13.182	0.0001
3rd volume	3.5625	1.22752	3.0442	4.0808	14.218	0.0001
1st count	32.9167	19.15365	24.8288	41.0045	8.419	
2nd count	33.3750	18.60297	25.5197	41.2303	8.789	0.0001
3rd count	43.8333	18.59562	35.9811	51.6856	11.548	0.0001
1st Active	16.1250	16.17919	9.2931	22.9569	4.883	
2nd active	17.7083	18.32195	9.9717	25.4450	4.735	0.0001
3rd active	17.5833	16.58946	10.5782	24.5884	5.192	0.0001
1st sluggish	31.7500	20.58545	23.0575	40.4425	7.556	
2nd sluggish	32.7083	16.95641	25.5483	39.8684	9.450	0.0001
3rd sluggish	36.2917	16.34540	29.3896	43.1937	10.877	0.0001
1st non	50.4167	21.99588	41.1286	59.7047	11.229	
2nd non	49.6250	20.17922	41.1041	58.1459	12.048	0.0001
3rd non	46.5417	17.30539	39.2342	53.8491	13.175	0.0001
1st Abnormal	51.0417	11.85228	46.0369	56.0464	21.097	
2nd abnormal	45.3333	10.03328	41.0967	49.5700	22.135	0.0001
3rd abnormal	43.3333	12.70627	37.9679	48.6987	16.707	0.0001

When we compare the whole population who recruited to the three strategies of treatment collectively as shown in Table 2 which showing significant association and correlation volume, a number of non-motile sperm at its three stages of examination and the also at there was a strong correlation for the shape of abnormal sperms at first stage. Other parameters don't show such an association.

Combination of L-argini and co-Enzyme showing the highest change in the total volume in the three occasions of measures, followed by L-Arginin then Co-Enzymes as shown in Figure 1.

Even though the was a slight increment in the volume between the 1st and the 2nd visit, there was the non-significant difference in the volume change according to the different treatment protocols at the three visit, where the p value > 0.05

Even though the count showing no very wide difference in their change between the three different modalities but the wider differences occurring in combination group followed by L-arginin then Co-Enzyme, where highest difference occurring in a group of combination.

There was high evidence graphically to increase the number of active sperms with the combination mode of treatment followed by L-arginin then the co-enzymes. As shown in Figure 3.

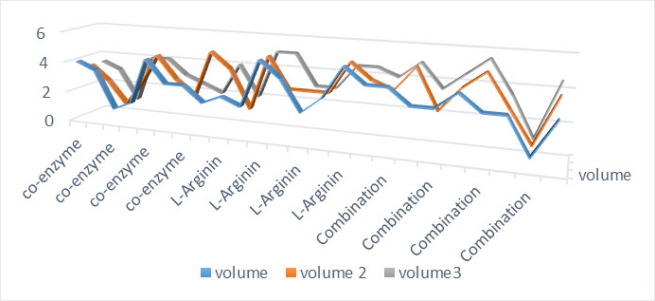

Figure 1: Distribution of volumes according to the modality of intervention

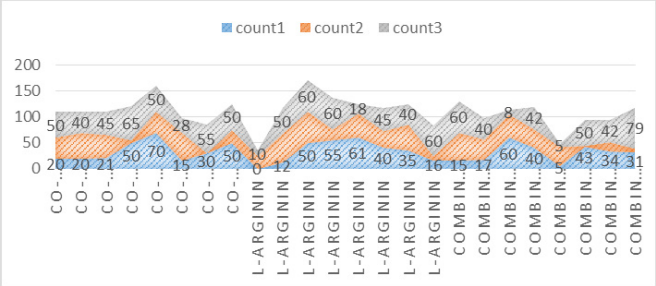

Figure 2: Distribution of sperm counts according to the modality of intervention

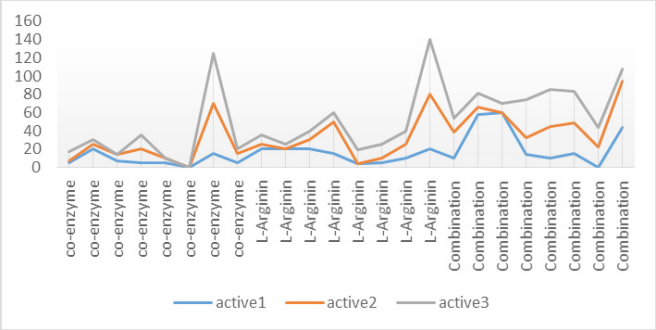

Figure 3: Distribution of active motile sperm according to treatment modalities

Table 2: Relationship and correlation of pairs of the parameter for the whole studied population

Pairs of comparisons		*Mean of difference*	*t*	*Sig.*	*Correlation*	*Sig lower*	*95% Confidence interval* *Upper*	
Pair 1	1st volume * 2nd volume2	1.03028	-1.337-	.194	.631	.001	-.71630-	.15380
Pair 2	1st volume* 3rd volume3	.92219	-2.601-	.016	.699	.0001	-.87899-	-.10018-
Pair 3	1st count * 2nd count2	28.03721	-.080-	.937	-.103-	.633	-12.29741-	11.38074
Pair 4	1st Count * 3rd Count	24.33269	-2.198-	.038	.169	.429	-21.19146-	-.64187-
Pair 5	1st Active* 2nd active	23.45007	-.331-	.744	.080	.709	-11.48543-	8.31876
Pair 6	1st Active**3rd active	22.90999	-.312-	.758	.023	.917	-11.13237-	8.21571
Pair 7	1st Sluggish * 2nd sluggish	22.07284	.018	.985	.229	.282	-9.23721-	9.40388
Pair 8	1st sluggish*3rd sluggish3	23.38338	-1.257-	.221	.185	.388	-15.87394-	3.87394
Pair 9	1st non* 2nd non	20.79607	1.168	.255	.505	.012	-3.82308-	13.73974
Pair 10	1st non*3rd non3	19.55964	1.545	.136	.500	.013	-2.09265-	14.42598
Pair 11	1st Abnormal * 2nd abnormal	13.92364	2.008	.056	.199	.352	-.17110-	11.58777
Pair 12	1st Abnormal *3rd abnormal	19.67227	1.920	.067	-.282-	.181	-.59854-	16.01520

Table 3: Change in the mean values of the volume among patients according to the three different strategies

	Type of treatment	*N*	*Mean*	*Std. deviation*	*t*	*p*
volume	co-enzyme	8	2.8125	1.22292		
	L-arginin	8	3.4375	1.23744	-1.016-	.327
	Combination	8	2.9688	1.00390	-0.276	0.762
volume2	co-enzyme	8	3.0000	1.30931		
	L-arginin	8	3.5625	1.17830	-.903-	.382
	Combination	8	3.5000	1.33631	-0.759	0.462
volume3	co-enzyme	8	2.8750	1.02644		
	L-arginin	8	3.8750	1.09381	-1.886-	.080
	Combination	8	3.9375	1.37419	-1.765	0.103

Figures 4 to 6 showing that there was evidence in the decrement of the abnormal shapes sperm, sluggish sperms, and non -motile sperms with combination, L-arginin and co-enzymes respectively.

There was a significant positive correlation of the independent parameters with the types of management modalities, where crossly examined by correlation regression, it was evident that all parameters except the counts are positively correlated by which p value <0.05.

DISCUSSION

Clinical trial including twenty-four males with a mean age of 27.34 ± 5.32 years, different residence and occupations, matched to a large extent for their age, residence, and occupation complaining of sub-fertility for their last life. Exposed to three different regimens of treatment, the semen parameters were the outcome of interest.

This study showing improvement in some sperm parameters, which comparable to the meta-analysis done by Sedigheh *et al*. studies which focused on antioxidant supplements "especially a combination of antioxidants" and its role in the effective improvement in some semen parameters of men complaining of infertility.[32]

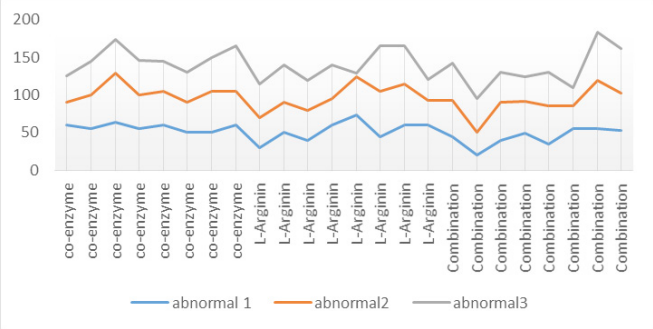

Figure 4: Distribution of abnormal shape sperm according to treatment modalities

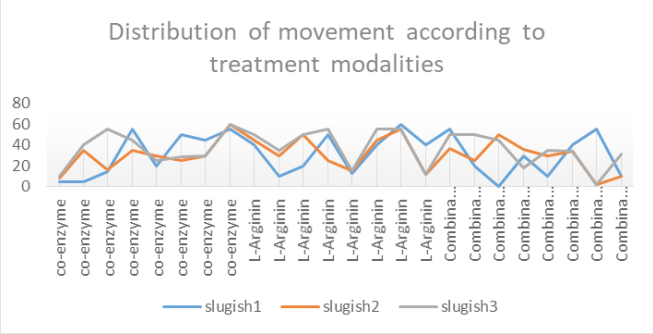

Figure 5: Distribution of movement according to treatment modalities

Table 4: Distribution of the count means according to the types of treatment

	Type of treatment	*N*	*Mean*	*Std. Deviation*
Count 1st	co-enzyme	8	34.5000	19.79899
	Combination	8	30.6250	17.73566
	L-Arginin	8	33.6250	22.12263
Count 2nd	co-enzyme	8	32.5000	20.52873
	Combination	8	30.3750	18.79922
	L-Arginin	8	37.2500	18.27371
Count 3rd	co-enzyme	8	47.8750	10.84221
	Combination	8	40.7500	24.70830
	L-Arginin	8	42.8750	19.43074

Overall changes

Regardless the type of treatment the semen volume at the three visits show significant difference especially at the last two visits (p = 0.0001), the combination of co-enzyme and L-arginin show high increment in the volume especially at the last visit, followed by L-arginin, then coenzyme, by correlation regression there was also very high significant statistical association for the second visit 0.631^{**} ($p < 0.01$) and for the third visit 0.699^{**}($p < 0.0001$), these results are comparable with Safarinejad *et al*. where they studied 228 patients with unexplained infertility, where they were with abnormal sperm motility, concentration, and morphology, underwent treatment for 28 weeks with anti-oxidant leading to improve the sperm volume, sperm count, motility and general morphology.[33]

Co-Enzyme Q10 group: in our study even though the was a slight increment in the volume between the 1st and the 2nd visit, there was non-significant difference in the volume change according to the different treatment protocols at the three visit, where the p-value > 0.05, and also Nadjarzadeh *et al*. who did a double-blind placebo-controlled clinical trial on forty-seven infertile men suffered from oligo-asthenic-terato-zoospermia,

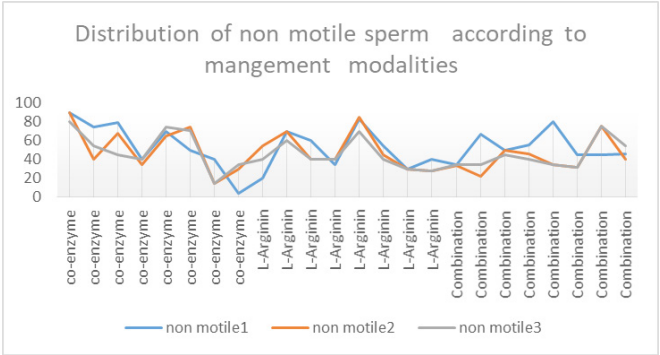

Figure 6: Distribution of non- motile sperm according to treatment modalities

Table 5: Correlation regression analysis of the parameters with the management modalities

Control Variables		*Correlation (r)*	*Significance (2-tailed) (P)*
1st Volume	Volume 2nd	0.631^{**}	0.001
	Volume 3rd	0.699^{**}	0.0001
1st Count	Count 2nd	-0.103-	0.633
	Count 3rd	0.169	0.429
1st Active	active2nd	0.023	0.917
	active3rd	0.761*	0.000
1st Sluggish	sluggish2nd	0.185	0.388
	sluggish3rd	0.708*	0.0001
1st Non	non2nd	0.505^{*}	0.012
	non3rd	0.500^{*}	0.013
1st Abnormal	Abnormal 2nd	0.421^{*}	0.041
	Abnormal 3rd	0.682*	0.003

who received 200 mg of CoQ10() daily or placebo at a period of the study. Non-Significant changes in semen parameters such as motility, or density and or morphology in the CoQ10 group, whereas total antioxidant capacity, was increased significantly ($p < 0.05$).[34,35] Our study is also consistent with Thakur, who suggests that semen parameters improved by 150 mg CoQ10-daily administration.[36] It is also compatible with the Lafuente R *et al*. meta-analysis shows that CoQ10 supplementing leading to global improvement in sperm parameters.[37]

L-Arginine

The sperm parameters regarding the volume, the sperm activity, and morphology show a highly evident significant difference among the three visits, where obvious increment had been noted. The p-value was < 0.001 at different levels, the values of means of the volume increased from 3.4 to 3.5 to 3.8, and for the counts jumped from 33.625 to 37.250 to 42.8750. The overall motility is also increased in a picture higher than that of the co-enzyme, but with a lesser extent to the parameter in the group exposed to combination protocol, the abnormally shaped sperm also decrease in a higher rate where the p-value was < 0.001, these finding are consistent with many studies using the L-arginie as enhancer of the male fertility Buzadzic *et al*. study, Petrovic´ V *et al*. study, Schulman SP *et al*. study, Stancic A *et al*. Study, Govers R *et al*. study and Stansilavov R *et al*. study.[38-43]

Combination of co-enzyme and L-arginine: In this study, there was an improvement in the whole volume, sperm activity, and motility and also decrease in the abnormal morphology. While the sperm count had no significant statistical differences at the three visits time, this was comparable to other studies, which where examine the supplementation of multiple antioxidants effect show an improvement in parameters of the semen after therapy.[44-46] For example, combination therapy with CoQ10 +carnitine, vitamin C and vitamin E for 3-6 months improved sperm concentration.[47] Only one study showed a significant improvement in sperm concentration after combination therapy without improvement in motility and morphology.[48-50]

Currently, multi-antioxidant supplementations are considered as an effective therapy for male infertility. The synergetic effect of multi antioxidants made them interesting for researchers; this was done by Galatioto *et al*.[51]

Abad and colleagues also carried out a study to determine the effect of oral antioxidant treatment upon the dynamics of sperm DNA fragmentation resulting in the proportion of DNA degraded sperm. And it was significantly reduced, and semen analysis data showed a significant increase in concentration, motility, vitality, and morphology parameters.[52]

Gopinath stated that the administration of antioxidants leads to a significant improvement in sperm count and total sperm motility.[50] Tremellen *et al*. conducted a prospective randomized, double-blind placebo-controlled trial resulting in the antioxidant group recorded a statistically significant improvement in viable pregnancy rates (38.5%) compared to the control group 16%.[52]

CONCLUSION

This study concluded that the administration of Co-Enzyme, L-arginine, and combination of both show improvement in most of the parameters of the semen. The combination was the first improver of the semen parameter followed by arginine, then the Co-Enzyme only, the volume, sperm morphology, and the activity were the main parameters affected by the multiple strategies of the treatment protocol.

Recommendation

Adding of the co-Enzyme to the protocol of the L-arginine as a good semen volume incrementer, activity enhancer, abnormal morphology reducer, further studies to determine the optimal dose of augmentation of both protocols is recommended, and finally a further studies is required for strict follow up of the patients who under tis treatment strategies about their wife if getting pregnancy or no

Limitations and difficulties

Follow up is the main difficulty in the study, the first limitation was the time of follow up, which no extending to know if the patient's wives are getting pregnancy or no.

Novelty and strength of the study

- It was the first clinical trial that done in our city, with full confidentiality and full written acceptance from all patients recruited in the study
- Role of augmentation of L-arginine by Co-enzyme Q10 had been achieved in most of the content of seminal fluid toward the good results.

REFERENCES

1. Evaluating Infertility-ACOG. Available at: https://www.acog.org/Patients/FAQs/Evaluating-Infertility?IsMobileSet=false. (Accessed: 22nd December 2018)
2. Idiopathic male infertility/Fertilitypedia. Available at: https://fertilitypedia.org/edu/diagnoses/idiopathic male-infertility#/Fertilitypedia-description. (Accessed: 22nd December 2018)
3. Gudeloglu, A., Brahmbhatt, J., & Parekattil, S. (2015). Definitions and epidemiology of unexplained male infertility. In Unexplained infertility (pp. 7-12). Springer, New York, NY. DOI:10.1007/978-1-4939-2140-9_2.
4. Farris, E. J. (1951). Male fertility. British medical journal, 2(4746), 1475.
5. L-Arginine & CoQ10 | Healthfully. Available at: https://healthfully.com/543410-l-arginine-coq10.html. (Accessed: 22nd December 2018).
6. Garg, H., & Kumar, R. (2015). Empirical drug therapy for idiopathic male infertility: what is the new evidence?. Urology, 86(6), 1065-1075.
7. Unexplained Infertility: State of the Science. Available at: https://www.medscape.com/viewarticle/767963. (Accessed: 22nd December 2018).
8. Infertility in Iraq and Afghanistan Veterans - Public Health. Available at: https://www.publichealth.va.gov/epidemiology/studies/new-generation/infertility.asp. (Accessed: 22nd December 2018).
9. McVeigh, E., Guillebaud, J., & Homburg, R. (2013). Oxford handbook of reproductive medicine and family planning. OUP Oxford. DOI:10.1093/med/9780199650682.001.0001.

10. Majzoub, A., & Agarwal, A. (2017). Antioxidant therapy in idiopathic oligoasthenoteratozoospermia. Indian journal of urology: IJU: journal of the Urological Society of India, 33(3), 207-214
11. WHO (2014). Infecundity, infertility, and childlessness in developing countries. Demographic and Health Surveys (DHS) Comparative reports No. 9. *WHO*.
12. Treating Infertility - ACOG. Available at: https://www.acog.org/Patients/FAQs/Treating-Infertility?IsMobileSet=false. (Accessed: 22nd December 2018).
13. Iraq Then and Now: A Guide to the Country and Its People - Karen Dabrowska, Geoff Hann - Google Books. Available at: https://books.google.iq/books?id=DhJ3lRnXyXcC&pg=PA262&redir_esc=y#v=onepage&q&f=false. (Accessed: 25th April 2018).
14. Thi Qar Governorate - Wikipedia. Available at: https://en.wikipedia.org/wiki/Dhi_Qar_Governorate. (Accessed: 25th April 2018).
15. Central Statistical Organization. Available at: http://www.cosit.gov.iq/en/. (Accessed: 25th April 2018).
16. World Health Organization. (2010). *WHO laboratory manual for the examination and processing of human semen*. World Health Organization.
17. Statistical Package for the Social Sciences (SPSS)? - Definition from Techopedia. Available at: https://www.techopedia.com/definition/12401/statistical-package-for-the-social-sciences-spss. (Accessed: 21st November 2017).
18. Demographics dictionary definition | demographics defined. Available at: http://www.yourdictionary.com/demographics. (Accessed: 26th April 2018).
19. Name | Define Name at Dictionary.com. Available at: http://www.dictionary.com/browse/name. (Accessed: 26th April 2018).
20. Age | Define Age at Dictionary.com. Available at: http://www.dictionary.com/browse/age. (Accessed: 26th April 2018).
21. Sex | Definition of Sex by Merriam-Webster. Available at: https://www.merriam-webster.com/dictionary/sex. (Accessed: 26th April 2018).
22. Cooper, T. G., Noonan, E., Von Eckardstein, S., Auger, J., Baker, H. W., Behre, H. M., ... & Vogelsong, K. M. (2010). World Health Organization reference values for human semen characteristics. Human reproduction update, 16(3), 231-245.
23. Male Infertility Workup: Laboratory Studies, Imaging Studies, Other Tests. Available at: https://emedicine.medscape.com/article/436829-workup. (Accessed: 22nd December 2018)
24. Fertility problems | Guidance and guidelines | NICE.
25. Arginine (L-arginine): Heart Benefits and Side Effects. Available at: https://www.webmd.com/heart/arginine-heart-benefits-and-side-effects#1. (Accessed: 22nd December 2018).
26. Healthy High-Arginine Foods. Available at: https://www.healthline.com/health/healthy-high-arginine-foods. (Accessed: 22nd December 2018).
27. CoQ10 (Coenzyme Q10): Health Benefits, Dosage, & Side Effects. Available at: https://www.webmd.com/diet/supplement-guide-coenzymeq10-coq10#1. (Accessed: 22nd December 2018).
28. Coenzyme Q10 - Mayo Clinic. Available at: https://www.mayoclinic.org/drugs-supplements-coenzyme-q10/art-20362602. (Accessed: 22nd December 2018).
29. Ahmadi, S., Bashiri, R., Ghadiri-Anari, A., & Nadjarzadeh, A. (2016). Antioxidant supplements and semen parameters: An evidence based review. International Journal of Reproductive BioMedicine, 14(12), 729-736.
30. Safarinejad, M. R., Safarinejad, S., Shafiei, N., & Safarinejad, S. (2012). Effects of the reduced form of coenzyme Q10 (ubiquinol) on semen parameters in men with idiopathic infertility: a double-blind, placebo controlled, randomized study. The Journal of urology, 188(2), 526-531. [PubMed].
31. Nadjarzadeh, A., Shidfar, F., Amirjannati, N., Vafa, M. R., Motevalian, S. A., Gohari, M. R., ... & Sadeghi, M. R. (2014). Effect of Coenzyme Q10 supplementation on antioxidant enzymes activity and oxidative stress of seminal plasma: a double-blind randomised clinical trial. Andrologia, 46(2), 177-183. [PubMed].
32. Nadjarzadeh, A, Sadeghi, M, Amirjannati, N, Vafa, M, Motevalian, S, Gohari, M, *et al*. (2011). Coenzyme Q10 improves seminal oxidative defense but does not affect on semen parameters in idiopathic oligoasthenoteratozoospermia: a randomized double-blind, placebo controlled trial. J Endocrin Invest. 34:e224–e228. [PubMed].
33. Thakur, A. S., Littarru, G. P., Funahashi, I., Painkara, U. S., Dange, N. S., & Chauhan, P. (2015). Effect of ubiquinol therapy on sperm parameters and serum testosterone levels in oligoasthenozoospermic infertile men. Journal of clinical and diagnostic research: JCDR, 9(9), BC01.–BC03. [PMC free article] [PubMed].
34. Lafuente, R., González-Comadrán, M., Solà, I., López, G., Brassesco, M., Carreras, R., & Checa, M. A. (2013). Coenzyme Q10 and male infertility: a meta-analysis. Journal of assisted reproduction and genetics, 30(9), 1147-1156. [PMC free article] [PubMed].
35. Buzadzic, B., Vucetic, M., Jankovic, A., Stancic, A., Korac, A., Korac, B., & Otasevic, V. (2015). New insights into male (in) fertility: the importance of NO. British journal of pharmacology, 172(6), 1455-1467.
36. Petrovic´ ,V, Korac, A, Buzadzic, B and Korac, B (2005). The effects of L-arginine and L-NAME supplementation on redox-regulation and thermogenesis in interscapular brown adipose tissue. J Exp Biol. 208: 4263–4271.
37. Schulman, SP, Becker, LC, Kass, DA, Champion, HC, Terrin, ML, Forman S *et al*. (2006). L-arginine therapy in myo-cardial infarction. The Vascular Interaction with Age in Myocardial Infarction (VINTAGE MI) randomized clinical trial. JAMA 295: 58–64.
38. Stancic, A, Korac, A, Buzadzic, B, Otasevic, V, Jankovic, A, Vucetic, M *et al*. (2012). L-Arginine in nutrition: multiple beneficial effects in the etiopathology of diabetes. J Nutr Ther 1: 114–131.
39. Govers, R and Oess, S (2004). To NO or not to NO: 'where?' is the question. Histol Histopathol 19: 585–605. Grimble GK (2007). Adverse gastrointestinal effects of arginine and related amino acids. J Nutr 37: 1693–1701.
40. Stansilavov, R and Rohdewald, P. (2014). Sperm quality in men is improved by supplement with a combination of L-arginine, L-citrullin, roburins, and Pycnogenol®. Minerva Urol Nefrol. 66(4): 217-223.
41. Galatioto, GP, Gravina, GL, Angelozzi, G, Sacchetti, A, Innominato, PF, Pace, G, *et al*. (2008). May antioxidant therapy improve sperm parameters of men with persistent oligospermia after retrograde embolization for varicocele? World J Urol. 26: 97–102. [PubMed].
42. Abad, C, Amengual, M, Gosálvez, J, Coward, K, Hannaoui N, Benet J, *et al*. (2013). Effects of oral antioxidant treatment upon the dynamics of human sperm DNA fragmentation and subpopulations of sperm with highly degraded DNA. Andrologia. 45:211–216. [PubMed].

43. Gopinath, P, Kalra, B, Saxena, A, Malik, S, Kochhar, K, Kalra, S, *et al*. (2013). Fixed Dose Combination Therapy of Antioxidants in Treatment of Idiopathic Oligoasthenozoospermia: Results of a Randomized, Double-blind, Placebo-controlled Clinical Trial. Int JInfertil Fetal Med. 4:6–13.
44. Gvozdjáková, A., Kucharská, J., Dubravicky, J., Mojto, V., & Singh, R. B. (2015). Coenzyme Q10, α-tocopherol, and oxidative stress could be important metabolic biomarkers of male infertility. Disease markers, 2015. ID 827941. [PMC free article] [PubMed].
45. Safarinejad, MR and Safarinejad, S. (2009). Efficacy of selenium and/or N-acetyl-cysteine for improving semen parameters in infertile men: a double-blind, placebo controlled, randomized study. J Urol. 181:741–751. [PubMed].
46. Ahmadi, S., Bashiri, R., Ghadiri-Anari, A., and Nadjarzadeh, A. (2016). Antioxidant supplements and semen parameters: An evidence based review. International Journal of Reproductive BioMedicine, 14(12), 729.
47. Majzoub, A., & Agarwal, A. (2018). 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, 16(1), 113-124. Published online 2018 Jan 2. doi: 10.1016/j.aju.2017.11.013.
48. Galatioto, G. P., Gravina, G. L., Angelozzi, G., Sacchetti, A., Innominato, P. F., Pace, G., ... & Vicentini, C. (2008). May antioxidant therapy improve sperm parameters of men with persistent oligospermia after retrograde embolization for varicocele?. World journal of urology, 26(1), 97-102. [PubMed].
49. Abad, C., Amengual, M. J., Gosálvez, J., Coward, K., Hannaoui, N., Benet, J., ... & Prats, J. (2013). Effects of oral antioxidant treatment upon the dynamics of human sperm DNA fragmentation and subpopulations of sperm with highly degraded DNA. Andrologia, 45(3), 211-216. [PubMed].
50. Gopinath, P., Kalra, B., Saxena, A., Malik, S., Kochhar, K., Kalra, S., & Zaveri, H. (2013). Fixed dose combination therapy of antioxidants in treatment of idiopathic oligoasthenozoospermia: results of a randomized, double-blind, placebo-controlled clinical trial. Int J Infertil Fetal Med, 4(4), 6-13.
51. Tremellen, K., Miari, G., Froiland, D., & Thompson, J. (2007). A randomised control trial examining the effect of an antioxidant (Menevit) on pregnancy outcome during IVF-ICSI treatment. Australian and New Zealand Journal of Obstetrics and Gynaecology, 47(3), 216-221. [PubMed].
52. Gvozdjáková, A., Kucharská, J., Dubravicky, J., Mojto, V., & Singh, R. B. (2015). Coenzyme Q10, α-tocopherol, and oxidative stress could be important metabolic biomarkers of male infertility. Disease markers, 2015. 2015:ID 827941. [PMC free article] [PubMed]