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THE EFFECT OF ALPHA LIPOIC ACID ON IDIOPATHIC ASTHENOZOOSPERMIC PATIENTS

By

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ABSTRACT

Background: Many infertile men have disorders correctable with the use of medication, and if diagnosed and treated properly, natural fertilization can be attained.

Objective: To evaluate the effect of ALA on semen parameters in idiopathic asthenozoospermia.

Patients and methods: This was a case-control study, including 80 patients presenting with primary infertility enrolled from outpatient Andrology Clinic Units of Al-Azhar University Hospitals. Patients were divided into two equal groups. One group was given oral ALA tablets at a dose of 300 mg twice/day, whereas the other group was given a placebo twice daily. The duration of the study ranged from March 2020 till September 2020.

Results: There was a significant difference between 2 groups as regard total motility after treatment progressive motility after treatment, and % vitality after treatment.

Conclusion: Medical therapy of asthenoteratospermia with ALA supplement could improve quality of semen parameters.

Keywords: Reproductive, Infertility, ALA, Semen, and Asthenozoospermia.

INTRODUCTION

Asthenozoospermia is a condition in which the percentage of progressively motile sperm is abnormally low. In men, it is defined as less than 25% rapid motility or less than 50% progression in a semen sample *(Lu et al., 2010)*.

Alpha-lipoic acid (ALA) is one of the most powerful biological antioxidants and is considered as a “universal antioxidant” due to both water and fat solubility. This antioxidant can easily penetrate different tissues, cells and even organelles such as mitochondria as main engine driving ROS production. Alpha-lipoic acid is an organo-sulphur compound (di-thiol) derived from octanoic acid and acts as a necessary cofactor for many enzymes. It can salvage other endog-enous (enzymatic and nonenzymatic) antioxidants such as oxidized vitamin C, glutathione, vitamin E, Coenzyme Q10 and even more (Borowczyk et al., 2015).

ALA has been used successfully in experimental animals to protect against the oxidative stress induced by X-ray and chemotherapeutic agents *(Manda et al., 2011)*.

The aim of the study was to evaluate the effect of ALA on semen parameters in idiopathic asthenozoospermia.

PATIENTS AND METHODS

This was a clinical trial, carried at outpatient Andrology clinic units of Al-Azhar University Hospitals from December 2019 till June 2020 eighty patients presenting with primary infertility were divided into two equal groups; 40 ALA and 40 placebo groups.

Inclusion criteria:

Infertile patients (more than 1 year) with asthenozoospermia (low motility: less than 32% progressive motility and less than 40% progressive and no progressive motility), normal FSH and testosterone levels.

Exclusion criteria:

Azoospermic patients, smoking, varicoceles patients (no varicocele by clinical examination & duplex), gonadotoxins and anti-androgens, alcoholics, endocrinal or genetic disorders, genitourinary tract infections chemotherapy and infertility therapy for 1 year.

Patients were subjected to history, physical examination and Semen analyses. The sample was collected after a minimum of 2 days and a maximum of 7 days of sexual abstinence. The result of semen analysis was compared to the standard values for semen analysis according to the criteria of *Lu et al. (2010)*. Colorimetric method was used for analyzing seminal total antioxidant capacity (TAC; biodiagnostic) *(Khosrowbeygi et al., 2012)*.

Total anti-oxidant capacity was measured in seminal plasma before the study and after treatment course for the two stuied groups.

Intervention: One group was given oral ALA tablets at a dose of 300 mg twice/day (Thiotacid 300 mg; Eva Company, Cairo, Egypt),whereas the other group was given a placebo twice daily. The duration of therapy for both groups was 3 months; semen analysis was assessed again in each group after termination of treatment.

An informed verbal consent from every participant was obtained.

Statistical analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level.

RESULTS

This table shows that there were significant difference between 2 groups as regard occupation and there were high significant difference between 2 groups as regard duration of marriage **(Table 1)**.

Table (1): Comparison between the two studied groups according to demographic data

Parameters \ Groups	Group A (n = 40)		Group B (n = 40)		P
	No.	%	No.	%	
Age (years)					
20 – 30	13	32.5	5	12.5	$^{MC}p=$ 0.077
30 – 40	23	57.5	32	80.0	
>40	4	10.0	3	7.5	
Min. – Max.	25.0 – 41.0		27.0 – 41.0		0.216
Mean ± SD.	33.88 ± 5.35		35.18 ± 3.86		
Median (IQR)	35.50 (29.0 – 38.0)		36.0 (33.0 – 38.0)		
Residence					
Urban	8	20.0	9	22.5	0.785
Rural	32	80.0	31	77.5	
Education Status					
Less than high school	10	25.0	7	17.5	0.670
High school	23	57.5	24	60.0	
Bachelor degree	7	17.5	9	22.5	
Occupation					
Worker	4	10.0	7	17.5	0.041
Employee	20	50.0	27	67.5	
Professional	16	40.0	6	15.0	
Duration of marriage					
Min. – Max.	2.0 – 6.0		2.0 – 9.0		0.001
Mean ± SD.	4.20 ± 1.42		5.73 ± 2.14		
Median (IQR)	4.0 (3.0 – 5.0)		6.0 (4.0 – 7.50)		

$\chi 2$: Chi square test, MC: Monte Carlo, t: Student t-test, U: Mann Whitney test
p: p value for comparing between the studied groups,*: Statistically significant at $p \leq 0.05$
Group A: cases group, Group B: placebo group

There is high significant difference between 2 groups as regard volume after treatment and there is significant difference between 2 groups as regard count before treatment and there is high significant difference between 2 groups as regard count after treatment. There is high significant difference between 2 groups as regard total motility after treatment and as regard progressive motility after treatment and as regard % vitality after treatment **(Table 2)**.

Table (2): Comparison between the two studied groups according to semen analysis

Semen analysis \ Groups		Group A (n = 40)	Group B (n = 40)	p
Volume (ml)	**Before treatment** Mean ± SD.	1.80 ± 0.64	1.76 ± 0.70	0.786
	After treatment Mean ± SD.	2.86 ± 0.79	1.75 ± 0.70	<0.001
	$^{t1}p_1$	<0.001	0.479	
Count x10^6/ml	**Before treatment** Mean ± SD.	15.17 ± 9.61	20.27 ± 10.18	0.031
	After treatment Mean ± SD.	47.96 ± 12.84	20.26 ± 10.36	<.0001
	$^{z}p_1$	<0.001	0.886	
Morphology (%)	**Before treatment** Mean ± SD.	3.97 ± 1.33	3.73 ± 1.34	0.421
	After treatment Mean ± SD.	4.59 ± 1.86	3.71 ± 1.35	0.064
	$^{z}p_1$	0.151	0.108	
Total Motility (%)	**Before treatment** Mean ± SD.	27.26 ± 13.59	23.49 ± 13.07	0.211
	After treatment Mean ± SD.	54.29 ± 8.51	23.71 ± 13.68	<0.001
	$^{z}p_1$	<0.001	0.619	
Progressive Motility (%)	**Before treatment** Mean ± SD.	20.69 ± 9.11	17.85 ± 9.27	0.182
	After treatment Mean ± SD.	42.43 ± 5.25	18.07 ± 9.56	<0.001
	$^{z}p_1$	<0.001	0.064	
% Vitality	**Before treatment** Mean ± SD.	61.79 ± 13.45	58.62 ± 14.91	0.320
	After treatment Mean ± SD.	71.53 ± 9.24	58.34 ± 14.90	<0.001
	$^{t1}p_1$	<0.001	0.125	

t: Student t-test, U: Mann Whitney test, t1: Paired t-test, Z: Wilcoxon signed ranks test
p: p value for comparing between the studied groups, p1: p value for comparing between Before treatment and After treatment
Group A: cases group, Group B: placebo group

There was a significant difference between 2 groups as regard fructose after treatment and as regard PH after treatment and as regard pus cells after treatment **(Fig 1 and 2)**.

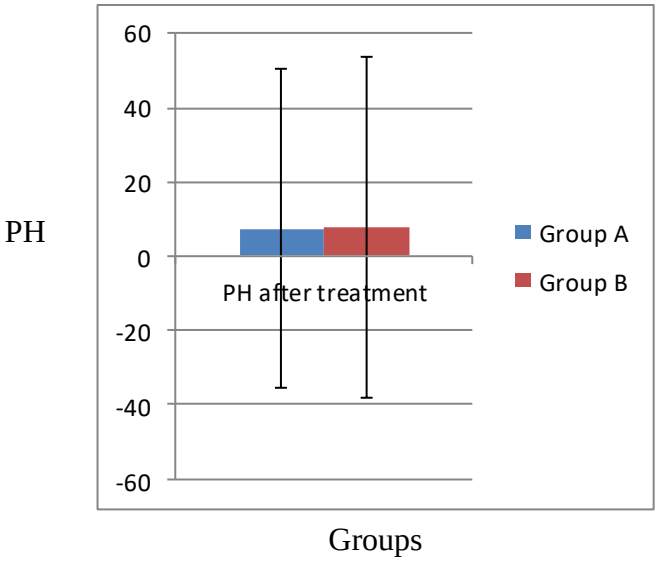

Figure (1): Comparison between the two studied groups according to PH after treatment

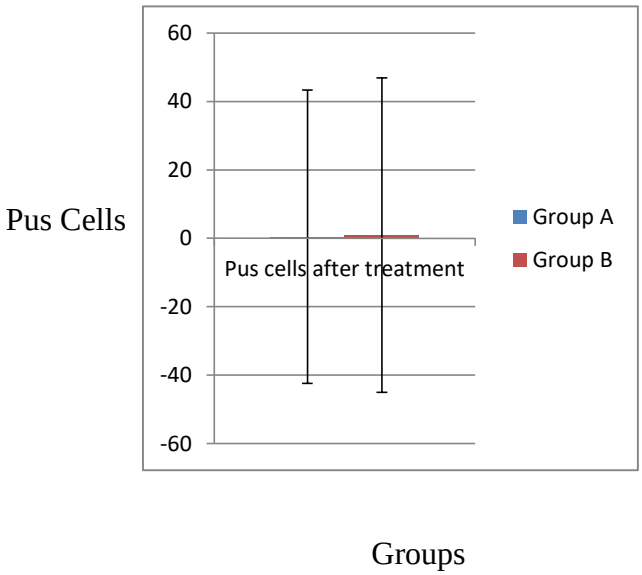

Figure (2): Comparison between the two studied groups according to pus cells after treatment

This table shows that there is high significant difference between 2 groups as regard TAC after treatment **(Table 3)**.

Table (3): Comparison between the two studied groups according TAC

Parameters \ Groups		Group A (n = 40)	Group B (n = 40)	p
TAC (mmol/L)	**Before treatment**			
	Min. – Max.	0.44 – 1.79	0.45 – 1.85	0.517
	Mean ± SD.	1.15 ± 0.41	1.21 ± 0.39	
	Median (IQR)	1.27 (0.77 – 1.48)	1.14 (0.96 – 1.54)	
	After treatment			
	Min. – Max.	1.13 – 2.43	0.42 – 1.89	<0.001*
	Mean ± SD.	1.79 ± 0.37	1.20 ± 0.40	
	Median (IQR)	1.77 (1.46 – 2.13)	1.16 (0.96 – 1.55)	
	$^{t1}p_1$	<0.001*	0.051	

DISCUSSION

ALA, and its reduced form, DHLA, is effective against conditions in which oxidative stress has a role. It shows beneficial effects in oxidative stress conditions because of its synergistic action with other antioxidants. ALA, which is a universal antioxidant, functions in both aqueous and membrane phases *(Tremellen, 2012).*

In the present work there was a significant difference between 2 groups as regard occupation and there was a high significant difference between 2 groups as regard duration of marriage. However, *Eslamian et al. (2015)* reported that there was no significant difference between the studied groups regarding age and duration of marriage.

The present study showed that there was no significant difference between 2 groups. As regard weight, height, and BMI.

Our results were in agreement with study of *Haghighian et al. (2015)* as they demonstrated that the three were no significant changes in BMI, weight, and physical activity in the subjects after consuming of ALA and placebo.

The current study showed that there was a high significant difference between 2 groups as regard volume after treatment and there was a significant difference between 2 groups as regard count before treatment. Our results were supported by study of *Haghighian et al. (2015)* as they reported that there were no significant differences in baseline levels of sperm concentration, sperm count, and sperm total motility between the two groups. However, ALA supplementation, compared with placebo, significantly increased sperm concentration and sperm count.

Furthermore, *Canepa et al. (2018)* showed a statistically significant increase of sperm concentration number of spermatozoa of total motile sperm count and normal sperm morphology after the treatment respect on the baseline.

In the study in our hands, there was a high significant difference between 2 groups as regard total motility after treatment and as regard progressive motility and % vitality after treatment. There was a significant difference between 2 groups as regard fructose and PH pus cells after treatment. Our results were in line with study of *Ibrahim et al. (2012)* as they reported that there was a significant change in sperm motility in all concentration used. However, the percentages of changes were different for each of the concentration groups. The percentage of motile sperm increased dramatically, from 112.8% to 251.0%. The increasing phase pattern change reversed following introduction of more concentrated solutions of ALA.

According to *Raaia et al. (2012),* they showed that ALA could work with its protective mechanisms (antioxidant and immune-modulator), enhancing the testicular function. According to previous studies with antioxidants, they expected an improvement mainly in sperm motility, but a surprising finding was the effect of the ALA on the count (P 0.001) after the third month of therapy; this could be related to the decrease in DNA fragmentation and the hypothesized protective role of the germ cells.

In the study of *Ibrahim et al. (2011),* the most significant changes on sperm motility could be seen in sperm population isolated after 2 and 4 minutes of separation. There was no much effect of both antioxidants (coenzyme Q10 (CoQ10) and ALA) on sperm population isolated at 6 minutes. Furthermore, *Buanayuda et al. (2019)* revealed that the higher progressive motility values in the sperm preparation group with ALA compared to the preparation group without ALA occurred after 3 hours of observation statistically significant, while the higher progressive motility values in the sperm preparation group with ALA compared with the control group from the start of the observation (0 hours). It was statistically significant and higher progressive motility values also occurred in the sperm preparation group without ALA compared to the control group from the initial observation (0 hours). *Yeni et al. (2012)* found that administration significant (P<.05) in some reproductive tract measures motility, membrane integrity, and abnormal rate of sperm in adult male rats compared with the placebo group.

The present study showed significant difference between 2 groups as regard TAC after treatment. Our results were supported by study of *Haghighian et al. (2015)* as they showed that seminal TAC and MDA levels were improved by ALA consumption and the quality of sperm and increased the TAC. *Bidmeshkipour et al. (2010)* results indicated that TAC levels in the seminal plasma of asthenospermic men were significantly lower than in healthy men. In addition, they found a positive correlation between reduced TAC levels and low sperm motility.

CONCLUSION

Supplementation with ALA can improve sperm quality. After treatment in oligoasthenoteratozoospermic men, mean count, concentration, and motility increased significantly compared with the placebo group.

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تأثير حمض ألفا ليبويك على مرضى ضعف حركة الحيوانات المنوية مجهول السبب

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خلفيـــة البحـــث: تشـــمل الأســـباب الهامـــة لعقـــم الـــذكور نـــزول النطـــاف، قلـــة النطـــاف, أو قصـــور الغـــدد التناســـلية. وقـــد أشـــارت الدراســـات إلـــى أنـــه يمكـــن التغلب على بعض مشاكل العقم من خلال تقنية الإنجاب المساعدة.

الهـــدف مـــن البحـــث: تقيـــيم تـــأثير أحمـــاض ألفـــا ليبويـــك على معلمـــات الســـائل المنوي في الوهن مجهول السبب.

المرضـــي وطـــرق البحـــث: تـــم إجـــراء هـــذه الدراســـة علـــي 80 مريضـــاً يعـــانون مـــن العقـــم الأولـــي المســـجلين مـــن وحـــدات العيـــادات الخارجيـــة لأمـــراض الـــذكورة بمستشـــفيات جامعـــة الأزهـــر, وتـــم تقســـيمهم إلـــى مجمـــوعتين متســـاويتن. أعطيـــت مجموعـــة واحـــدة أقـــراص أحمـــاض ألفـــا ليبويـــك عـــن طريـــق الفـــم بجرعـــة 300 ملـــغ مـــرتين فـــي اليـــوم بينمـــا أعطيـــت المجموعـــة الأخـــرى دواء وهمـــي مـــرتين يوميًـــا. تراوحـــت مـــدة الدراســـة مـــن شـــهر مارس 2020 وحتى شهر سبتمبر 2020.

نتـــائج البحـــث: كـــان هنـــاك اختلافًـــا كبيـــرًا بـــين مجمـــوعتين فيمـــا يتعلـــق بالمهنـــة، وكـــان هنـــاك اختلافًـــا كبيـــرًا بـــين مجمـــوعتين فيمـــا يتعلـــق بمـــدة الـــزواج. ولـــم يكـــن هنـــاك فـــرق كبيـــر بـــين مجمـــوعتين فيمـــا يتعلـــق بالتـــاريخ الماضـــي والاعـــتلال المشـــترك. وهنـــاك فـــرق كبيـــر بـــين مجمـــوعتين فيمـــا يتعلـــق بـــالحجم بعـــد العـــلاج، كمـــا أن هنـــاك فـــرق كبيـــر بـــين مجمـــوعتين فيمـــا

يتعلق بالعد قبل العلاج وفرق كبير بين مجموعتين فيما يتعلق بعد العلاج. وهناك فرق كبير بين مجموعتين فيما يتعلق بالحركة الكلية بعد العلاج وفيما يتعلق بالحركة التقدمية بعد العلاج وفيما يتعلق بنسبة الحيوية بعد العلاج. وهناك فرق كبير بين مجموعتين فيما يتعلق بالفركتوز بعد العلاج وفيما يتعلق بالحموضه بعد العلاج وفيما يتعلق بالخلايا الصديد بعد العلاج.

الإستنتاج: التركيز الأمثل لأحماض ألفا ليبويك قادر على تحسين حركة الحيوانات المنوية وحيويتها وتقليل تلف الحمض النووي.