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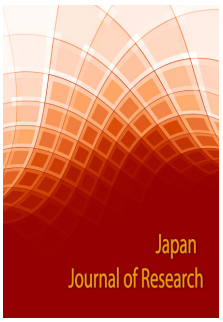

Evaluating the Impact of Cyclofert Male™ Supplement on Sperm Parameters and Male Fertility: A Prospective Real-World Study in Lebanese Men

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Abstract

This prospective observational study assesses the impact of Cyclofert Male™, a supplement containing antioxidants and micronutrients, on sperm parameters among forty-nine Lebanese men with sub-fertility. Over six months, participants showed significant improvements in sperm density, progressive motility, morphology although sperm volume remained unchanged. Pregnancy rates were 18% at three month and 29% at month six. This observational real world data study highlights the benefits of antioxidants like L-carnitine, CoQ10, zinc and N-acetyl-cysteine in improving male fertility, with Cyclofert Male™ showing promising results. Limitations include the small sample size, localized setting, and lack of stratification by socioeconomic factors. Larger studies are recommended for further validation.

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Introduction

The World Health Organization (WHO) defines infertility as the inability to conceive children after one year of regular unprotected intercourse [1]. Male infertility is one of the most common causes of infertility, accounting for around 30% of infertility cases [2]. More than 90% of male infertility cases are caused by low sperm count, poor sperm quality, or both [3]. Obstructive azoospermia is caused by a blockage in the vas deferens preventing the passage of sperm, while non-obstructive azoospermia is caused by an inability to produce sperm [3]. Infertility can also be caused by ejaculatory problems (retrograde ejaculation or anejaculation) [4]. Hypogonadism is another cause of infertility, wherein low levels of testosterone cause an insufficient secretion of gonadotrophic-releasing hormone and/or gonadotrophin secretion, thus low sperm count [5].

There are various treatment modalities for male infertility. These include hormonal therapies (gonadotropin-releasing hormone, gonadotropin, aromatase inhibitors, selective estrogen modulators, and dopamine agonists), surgical sperm extraction, and antioxidants [6]. Oxidation has been shown to increase the rates of male infertility when reactive oxygen species were present [7]. As a results, antioxidant treatment has been widely considered. Even though studies on effectiveness and efficacy of antioxidants on sperm and pregnancy are still limited, literature has documented contradictory results. A combination of vitamins E and C did not improve rates of pregnancy or semen parameters, however it showed a meaningful reduction in the rates of deoxyribonucleic acid (DNA) fragmentation caused by reactive oxygen species [8,9]. Another systemic review found that oral antioxidants (vitamins C and E, zinc, selenium, folate, carnitine, and carotenoids) had beneficial outcome in some cases of infertility in improving pregnancy rates and sperm parameters, however the results were not the same among all studies included [10].

Cyclofert™ Male is a food supplement containing essential compounds required for DNA synthesis and spermatogenesis. These compounds are l-carnitine l-tartrate, N – Acetyl cysteine, zinc, lycopene, vitamins E and C, glutathione, selenium, coenzyme Q10, and folic acid. Antioxidants such as vitamin E, glutathione, and coenzyme Q10 protect sperm from oxidative stress and improve motility [11]. L-carnitine supports energy production essential for sperm movement, while selenium and zinc play crucial roles in DNA protection and overall sperm function [11]. Folic acid aids in DNA synthesis and antioxidant defense, and lycopene provides potent protection against oxidative damage. This blend of nutrients aims to optimize sperm parameters and support male fertility [11].

The aim of this study is to explore the effect of Cyclofert Male™ on sperm parameters among a cohort of Lebanese population experiencing male infertility.

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Methodology

This is a prospective observational real world study. Patients were recruited from the urology department in a private hospital in Beirut, Lebanon between December 2002 and February 2024. Patients included were aged 20 to 60 years old, had sub-fertility, primary infertility one year or more, secondary infertility two years or more, the couple were not using any form of contraception, had no disease affecting their fertility, had sperm count <20 million/ml, forward sperm progressive motility <20%, normal sperm morphology <10%, and patients had normal semen liquefaction (<5 minutes). Participants were excluded if they had obstructive or non-obstructive azoospermia, disease affecting sperm parameters, or had seminal infection. Patients were instructed to consume 2 tablets of Cyclofert Male™ per day for a period of 6 months. Ethical approval for this study was obtained from the Urology Department at Levant Hospital, Beirut – Lebanon and written informed consent was obtained from all participants prior to their inclusion in the study.

Data Collection

Data were collected at baseline before treatment initiation, 3 months, and 6 months post-treatment. Variables included age, urbanicity, smoking status, alcohol intake, comorbidities. Sperm parameters were also collected including sperm volume, density, overall progressive motility, fast and slow progressive motility, normal morphology, and rate of pregnancy.

Data Analysis

Analysis was performed using STATA 18. Descriptive statistics were initially conducted for sociodemographic and clinical characteristics in addition to sperm parameters using the frequency and corresponding valid percentage. In order to explore any meaningful changes in sperm parameters, mixed models regression was used since it has a better performance on smaller sample size and performs better with missing data. Statistical significance was assumed at p-value <0.005.

Results

Demographic and Clinical Characteristics

The sample consists of 49 individuals with an average age of 32.63 years (±7.74). Urban residents constitute 74.47% of the sample, while rural residents make up 25.53%. Among the participants, 42.86% are smokers, and 16.33% consume alcohol. The average BMI is 27.49 (±3.70). Regarding health conditions, 4.08% have cardiovascular diseases, 12.24% have diabetes, 14.29% have hypertension, and 6.12% have thyroid diseases. No participants reported having cancer, renal, liver, or hematological diseases. Other diseases were reported by 14.29% of the sample.

Table 1. *Demographic and clinical characteristics of the sample*

Total sample=49	
Age	32.63±7.74
Urbanicity Urban Rural	 35(74.47%) 12(25.53%)
Smoker	21(42.86%)
Alcohol	8(16.33%)
BMI	27.49±3.70
Cardiovascular diseases	2(4.08%)
Cancer	0(0)
Diabetes	6(12.24%)
Hypertension	7(14.29%)
Renal diseases	0(0)
Liver diseases	0(0)
Thyroid diseases	3(6.12%)
Hematological diseases	0(0)
Other diseases	7(14.29%)

Sperm Samples Characteristics

Regarding the sperm samples, the data showed that the sperm volume remained relatively stable across the three visits, with values of 2.78±0.98 ml at baseline, 2.78±0.82 ml at 3 months, and 2.74±0.54 ml at 6 months. In contrast, sperm density showed a significant increase from 14.73±14.59 million/ml at baseline to 25.55±26.28 million/ml at 3 months, followed by a slight decrease to 25.11±15.43 million/ml at 6 months. The overall progressive motility improved markedly, rising from 23.22±8.95% at baseline to 38.46±15.24% at 3 months, with a slight decrease to 35.15±10.92% at 6 months. Fast progressive motility also showed a consistent increase from 20.11±16.84% at baseline to 29.50±13.86% at 3 months and further to 35.55±15.54% at 6 months. Conversely, slow progressive motility decreased from 60.85±28.59% at baseline to 51.96±23.80% at 3 months and further to 50.74±20.53% at 6 months. Finally, the normal morphology of sperm significantly improved over time, increasing from 23.19±17.30% at baseline to 37.26±17.17% at 3 months and reaching 43.07±16.54% at 6 months. Additionally, pregnancy rates improved over time, with no pregnancies reported at baseline, 18.37% at 3 months, and 28.75% at 6 months.

Table 2. *Specimen characteristics at baseline, 3 months, and 6 months*

Variable	Visit 1	Visit 2	Visit 3
Sperm volume (ml)	2.78±0.98	2.78±0.82	2.74±0.54
Sperm density (mio/ml)	14.73±14.59	25.55±26.28	25.11±15.43
Overall progressive motility (%)	23.22±8.95	38.46±15.24	35.15±10.92
Fast progressive motility (%)	20.11±16.84	29.50±13.86	35.55±15.54
Slow progressive motility (%)	60.85±28.59	51.96±23.80	50.74±20.53
Normal morphology (%)	23.19±17.30	37.26±17.17	43.07±16.54
Pregnancy	0(0)	9(18.37%)	14(28.75%)

Table 3. *Specimen characteristics at baseline, 3 months, and 6 months*

	Sperm volume	Sperm density	Overall progressive motility	Fast progressive motility	Slow progressive motility	Normal morphology
Visit						
Coefficient	0.03	6.55	6.81	7.79	-7.08	10.87
95% CI	-0.11;0.17	2.25;10.85	3.07;10.55	4.31;11.28	-12.15; -2.02	7.21;14.53
P-value	0.67	0.003	<0.001	<0.001	0.006	<0.001
Age						
Coefficient	0.002	0.55	-0.34	0.26	0.21	0.21
95% CI	-0.01;0.02	0.03;1.07	-0.89;0.19	-0.16;0.68	-0.40;0.82	-0.23;0.65
P-value	0.79	0.03	0.21	0.22	0.51	0.35
BMI						
Coefficient	0.03	-0.05	0.37	0.71	-0.34	-0.09
95% CI	-0.01;0.07	-1.36;1.27	-0.78;1.52	-0.36;1.77	-1.89;1.21	-1.19;1.02
P-value	0.21	0.94	0.53	0.19	0.67	0.88
Smoking						
Coefficient	-0.29	0.72	0.69	0.85	-17.57	5.68
95% CI	-0.58; -0.02	-7.55;8.99	-5.83;7.22	-5.85;7.55	-27.31; -7.82	-1.32;12.69
P-value	0.03	0.86	0.83	0.8	<0.001	0.11
Alcohol						
Coefficient	0.06	-0.18	-5.48	4.9	7.86	0.99
95% CI	-0.31;0.43	-11.72;11.37	-15.01;4.05	-4.45;14.25	-5.74;21.46	-8.75;10.73
P-value	0.75	0.98	0.26	0.3	0.28	0.84
Chronic disease[1]						
Coefficient	-0.43	-13.56	-2.86	-10.59	12.55	-12.19
95% CI	-0.76; -0.09	-23.59; -3.54	-11.83;6.11	-18.71; -2.47	0.73;24.36	-20.66; -3.72
P-value	0.01	0.008	0.53	0.01	0.03	0.005

[1]Chronic disease as binary variable

Mixed Model

Change in biomarkers was statistically significant in sperm density, progressive motility (overall, slow, and fast), and in the percentage of normal morphology. For sperm volume, the coefficients indicate no significant change associated with visits (Coefficient = 0.03, 95% CI [-0.11, 0.17], P-value = 0.67), age, BMI, or alcohol consumption, while a significant decrease is associated with smoking (Coefficient = -0.29, 95% CI [-0.58, -0.02], P-value = 0.03) and chronic disease (Coefficient = -0.43, 95% CI [-0.76, -0.09], P-value = 0.01). For sperm density, visits are associated with a significant increase (Coefficient = 6.55, 95% CI [2.25, 10.85], P-value = 0.003), as is age (Coefficient = 0.55, 95% CI [0.03, 1.07], P-value = 0.03), while chronic disease is associated with a significant decrease (Coefficient = -13.56, 95% CI [-23.59, -3.54], P-value = 0.008). Other factors like BMI, smoking, and alcohol do not show significant associations with sperm density. For overall progressive motility, significant increases are associated with visits (Coefficient = 6.81, 95% CI [3.07, 10.55], P-value < 0.001), and significant decreases are associated with chronic disease (Coefficient = -2.86, 95% CI [-11.83, 6.11], P-value = 0.53). Fast progressive motility significantly increases with visits (Coefficient = 7.79, 95% CI [4.31, 11.28], P-value < 0.001) and significantly decreases with chronic disease. Slow progressive motility decreases significantly with visits (Coefficient = -7.08, 95% CI [-12.15, -2.02], P-value = 0.006) and smoking (Coefficient = -17.57, 95% CI [-27.31, -7.82], P-value < 0.001), while it increases significantly with chronic disease (Coefficient = 12.55, 95% CI [0.73, 24.36], P-value = 0.03). Lastly, normal morphology shows a significant increase with visits (Coefficient = 10.87, 95% CI [7.21, 14.53], P-value < 0.001) and a significant decrease with chronic disease (Coefficient = -12.19, 95% CI [-20.66, -3.72], P-value = 0.005). Other factors, such as age, BMI, and alcohol, do not show significant associations across most sperm characteristics.

Discussion

This study aimed to assess the effect of Cyclofert Male™ on sperm parameters among a cohort of patients with sub-fertility using real world laboratory data. Our findings show that all sperm parameters have significantly improved over 6 months

compared to data at 3 months and baseline, with exception to the sperm volume.

Several studies have assessed the individual effects of various antioxidants on sperm parameters. Lenzi et al showed that L-carnitine had a positive impact on sperm mobility among infertile men and that this relationship was more significant when baseline motility was lower [12]. Another study on carnitine, acetyl carnitine, or a combination of both, showed that carnitine and acetyl carnitine increased sperm motility and free radical scavenging capacity, and that 5 pregnancies out of 60 treated patients occurred due to these micronutrients [13].

After CoQ10 supplementation, Balercia et al showed an increased in sperm motility and semen and that twelve spontaneous pregnancies have occurred subsequent to supplementation [14].

A study by Hadwan et al showed the importance of zin supplementation on sperm parameters. After supplementing 37 infertile men with daily zinc, volume of semen, progressive sperm motility percentage and total normal sperm count have increased [15].

Safarinejad et al studied the impact of selenium and N-acetyl-cysteine on 468 infertile men with idiopathic oligo-asthenoteratospermia over 30 weeks, finding that treatment led to reduced serum follicle-stimulating hormone, increased serum testosterone and Inhibin B, and significant improvements in all semen parameters [16].

All these studies have found results similar to ours, however our study investigated a multi-antioxidant supplementation. Similar to the above, we found a significant increase in overall motility from 23.22% to 35.15%, normal morphology from 23.19% to 43.07%, and pregnancy rates to 28.75% by the 6th month.

This shows that antioxidants such as Cyclofert Male™ play an important in improving sperm parameters and thus fertility characteristics.

However, our study is not without limitation. In our sample, we did not account for all socioeconomic categories. Our sample is only from a private hospital and no patients were recruited from public hospitals. We only accounted for patients in the Lebanese capital, Beirut and not for other governorates. Our study could benefit from a larger, more representative sample. Moreover, we did not stratify by the various causes of infertility except in our exclusion criteria wherein we did not recruit obstruct and non-obstruct azoospermia.

Conclusions

This study shows that Cyclofert Male™ significantly improves sperm parameters and fertility rates in men with sub-fertility. Based on these findings, Cyclofert Male™ should be considered a potential supplement in male infertility treatment, especially for those affected by oxidative stress and unexplained causes of infertility. Further research with larger samples and longer follow-up is recommended to confirm these results.

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