The effect of an antioxidant agent-multivitamin complex food supplement on spermiogram in infertile men

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ABSTRACT

Objective: Oxidative stress (OS) occurs due to overproduction of reactive oxygen radicals (ROS) or weakening of anti-oxidant mechanisms and may harm fertility. Our study aimed to investigate the effects of combined support therapy containing antioxidant agents and vitamin complexes on fertility.

Materials and methods: In this retrospective case-control study, 300 randomly selected infertile men were included. For four months, the effect of daily intake of an antioxidant-multivitamin complex containing astaxanthin (5mg), Coenzyme Q10 (100mg), L-Arginine (250mg), L-Carnitine (250mg), Selenium (100mcg), Zinc (10mg), Folic acid (400mcg), Vitamin E (100mg) and Vitamin C (100mg) on spermiogram parameters was investigated.

Results: In semen volume (2.21 ml vs. 3.05 ml; p=.004), sperm concentration (9.60 million/ml vs. 14.10 million/ml; p=.000), progressive motility sperm count (16.50% vs. 26.65%; p=.000), sperm vitality rate (48% vs. 68%; p=.001) in patients receiving nutritional support a statistically significant increase was found. In addition, it was determined that the treatment provided a significant decrease (77% vs. 61%; p=.002) in the number of patients with abnormal morphology (at least 4% of patients who could not achieve normal morphology according to Kruger criteria).

Conclusion: It was determined that antioxidant-multivitamin-containing nutritional supplements containing Astaxanthin, Coenzyme Q10, L-arginine, L-carnitine, selenium, zinc, vitamins E and C provided significant improvement on semen volume, sperm morphology, vitality and motility. In this context, we predict that the antioxidant-multivitamin complex can be used as a food supplement for supportive treatment in male infertility.

Keywords: male infertility; astaxanthin; oxidative stress; spermiogram

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Introduction

Infertility is defined as the inability to achieve clinical pregnancy success within 12 months despite regular unprotected sexual intercourse, which is seen in 15% of couples [1,2]. Subfertility is defined as difficulty and delay in spontaneous fertilization [3,4]. The most critical parameter that can predict the possibility of unexpected pregnancy is the time that couples spend without using contraception due to their desire for fertility. The chance of pregnancy with regular intercourse in the first six cycles is approximately 80% [4]. The role of the male in fertility depends on the production of functional spermatozoa [1]. Decreased motility (asthenospermia), abnormal morphology (teratozoospermia), reduced number (oligospermia), or absence of sperm in the ejaculate (azoospermia) reduces the chance of pregnancy [5].

The role of oxidative stress (OS) on female and male fertility has gained importance in recent years and has begun to be understood [9]. The adverse effects of ROS on reproductive cells have begun to be understood [9]. The efficacy of various antioxidant agents, which increase the fertility capacity of infertile women and men, and nutritional supplements containing vitamins and minerals with known antioxidant activity have been demonstrated. In this context, many studies in the literature report the positive effects of Astaxanthin, Coenzyme Q10, Glutathione, L-Arginine, L-Carnitine, Selenium, Zinc, Vitamin E and Vitamin C on fertility [7,10-13].

Our study aimed to investigate the effects of combined support therapy containing antioxidant agents and vitamin complexes on fertility.

Material and methods

This study was carried out in the Department of Obstetrics and Gynecology, University of Health Sciences, Tepeçik Training and Research Hospital, a tertiary center. In this study, spermiogram data of 300 infertile men randomly selected among the patients treated in our infertility clinic between March and June 2022 were used. The retrospective study we conducted has been approved by the ethics committee on January 11, 2023, under research number 810 and decision number 830.
In the design and implementation of the study, the articles of the Helsinki Convention were adhered to. Male patients aged 18-55 years, without any systemic disease, and who had not taken any urological medicine or undergone surgery in the last six months were included in the study. Sperm samples were taken after at least three days of sexual abstinence. Volume, sperm concentration, total sperm count, total motility percentage, progressive motility percentage, morphology and vitality parameters were evaluated according to WHO 2010 criteria [14].

First and foremost, our study focused on examining the impact of a daily intake of an antioxidant-multivitamin complex on spermiogram parameters among our 150 patients. This complex contains astaxhantin (5mg), Coenzyme Q10 (100mg), L-Arginine (250mg), L-Carnitine (250mg), Selenium (100mcg), Zinc (10mg), Folic acid (400mcg), Vitamin E (100mg), and Vitamin C (100mg). Our primary aim was to observe potential improvements in sperm quality over a four-month period. We comparatively analyzed volume, concentration, total motility, progressive motility, abnormal morphology, and vitality parameters in spermiogram tests. These tests were taken from patients at the beginning and again at the end of the 4th month.

On the other hand, 150 patients whose mean age was similar to the study group and who did not want to use nutritional supplements were included in the control group. At the end of the 4th month, the volume, concentration, total motility and progressive motility parameters in the spermiogram tests taken from 300 patients, 150 of whom were from the study group and 150 from the control group, were ranked according to their numerical values. The patients were divided into two groups according to the median value of each parameter. The group of 150 people below the median value was called GROUP I, and the group of 150 people above the median value was called GROUP II. The proportions of patients using antioxidant-multivitamin complex in both groups were calculated and the statistical significance of the distribution was analyzed.

**Statistical analysis**

Statistical Package for Social Sciences (SPSS) 26.0 software program was used to analyze the data of the patients included in the study. Wilcoxon Signed Ranks Test was applied to examine the effect of the patients on the values before and after the drug. Pearson Chi-Square test was used to examine the relationship between the groups.

**Results**

In this study, it was determined that using antioxidant agent-multivitamin complex for 4 months significantly improved spermiogram parameters. In Semen volume (2.21 ml -3.05 ml; p=0.004), sperm concentration (9.60 million/ml -14.10 million/ml; p=0.000), progressive motility sperm count (16.50% -26.65%; p=0.000), sperm vitality rate (48% -68%; p=0.001) in patients receiving nutritional support a statistically significant increase was found. There was an increase in the total motile sperm count (36.65% -37.50%; p=0.006). In addition, it was found that the treatment provided a significant decrease (77% - 61%; p=0.002) in the number of patients with abnormal morphology (patients who could not achieve at least 4% normal morphology according to Kruger criteria) (Table 1).

Table 2 compares those who take nutritional supplements and those who do not. Accordingly, a statistically significant association was found between dietary supplement intake and increased sperm volume, concentration, progressive and total motile sperm count. According to this, 65% (n=97; p=0.000) of the patients whose sperm volume was above the median value, 70% (n=105; p=0.000) of the patients whose sperm concentration was above the median value and respectively 72% (n=108; p=0.000) and 80% (n=120; p=0.001) of the patients whose total and progressively mobile sperm count was above the median value were found to use antioxidant agent-multivitamin complex (Table 2).

**Discussion**

Although the exact cause of suboptimal semen quality is not clearly understood, environmental factors, mainly caused by oxidative stress, are blamed as well as genetic factors [15]. Studies have reported a negative correlation between the amount of ROS and the proportion of sperm with normal and borderline morphology [16, 18].

Assisted reproductive techniques can overcome infertility due to tubal factors or low sperm count. However, little progress has been made regarding the adverse effects of advancing age on ovarian function [1]. There are theories stating that this change in oocytes occurs secondary to increased oxidative stress and ROS imbalance secondary to abnormal vascularization and decreased perfusion [19]. PCOS, hyperglycemia, obesity, and endometriosis increase ROS in women [6,20].

There are many studies in the literature on the positive effects of antioxidant agents on fertility. Evaluated as a powerful antioxidant, Astaxhantin is a yellow-orange oil-soluble natural carotenoid. In addition to its antioxidant effect, it has attracted wide attention with its anti-inflammatory, anti-apoptotic and immunomodulatory properties. It has been used as a multi-purpose pharmacological agent in various diseases [21]. It has been reported to protect against oxidative stress by supporting the mitochondrial redox system [22]. It has been reported that astaxhantin protects sperm capacitation and has a protective and beneficial effect on sperm quality [23-25]. Studies have reported that astaxhantin supports blastocyst development and protects the oocyte against oxidative stress [26].

Coenzyme Q10, which has an antioxidant effect, improved the number of motile sperm and increased fertilization with

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**Table 1. Effect of antioxidant agent-multivitamin food complex on spermiogram**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before Treatment</th>
<th>After Medication</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age/year</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume/ml</td>
<td>2.21</td>
<td>3.05</td>
<td>0.004</td>
</tr>
<tr>
<td>Concentration/10⁶/ml</td>
<td>9.6</td>
<td>14.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Motility/%</td>
<td>36.65</td>
<td>37.5</td>
<td>0.006</td>
</tr>
<tr>
<td>Progressive Motility/%</td>
<td>16.5</td>
<td>26.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abnormal Morphology/%</td>
<td>77</td>
<td>61</td>
<td>0.002</td>
</tr>
<tr>
<td>Vitality/%</td>
<td>48</td>
<td>68</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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**Table 2. Antioxidant agent-multivitamin complex usage rate between groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group I (n=150)</th>
<th>Group II (n=150)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (n)</td>
<td>53(35%)</td>
<td>97(65%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Concentration (n)</td>
<td>45(30%)</td>
<td>105(70%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Motility (n)</td>
<td>42(28%)</td>
<td>108(72%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Progressive Motility (n)</td>
<td>30(20%)</td>
<td>120(80%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
spontaneous and assisted reproductive treatment methods. Similarly, a positive impact on fertility was found in women by increasing serum inhibit B levels and decreasing FSH levels [7,27-29].

Studies on subfertile men have reported improvement in sperm parameters with daily use of arginine, a semi-essential amino acid [7,30,31]. L-carnitine has a strong antioxidant effect as well as an energy support for the cell. It effects on motility by taking part in the transition of transportable fatty acids from the cytosol to the mitochondria. The use of carnitine has been associated with increased sperm motility and decreased ROS levels. It has been reported to have beneficial effects in treating female infertility [7,32-34].

Selenium is an antioxidant trace element that acts on glutathione peroxidase, by using its which Increased sperm motility has been reported [7,35,36]. Zinc is an essential micromineral found in the body, especially in the prostate gland, 2-4 mg. It is involved in repairing DNA damage. It is involved in testicular development and spermatogenesis. Its deficiency causes hypogonadism, testicular- seminiferous tubule atrophy, and retardation in developing secondary sexual character. [7,37,38] Seminal zinc deficiency may be a risk factor for sperm abnormalities and idiopathic male infertility. Infertile men who smoke are at risk for zinc deficiency. Zinc acts as an antioxidant against oxidative stress, which increases in smoking men. Poor nutritional status from zinc is a risk factor for poor sperm quality and idiopathic infertility [39]. Vitamin E and Vitamin C are water-soluble antioxidants. Degeneration of testicular germinal epithelium is detected in vitamin C deficiency. Ascorbic acids increase the effectiveness of gonadotropic treatments. It is recommended to use 90 mg daily. A reduction in sperm DNA damage has been reported with the combined use of vitamins C and E for two months [7,40]. Adequate intake of folic acid, vitamin C, vitamin E and selenium have been reported to have a protective effect on fertility [41]. Improvement in sperm parameters was observed in infertile men with supportive treatment consisting of L-carnitine, coenzyme Q-10, selenium, vitamins C and E, zinc and folic acid; It has been determined that it provides an increase in fertility by strengthening the antioxidative system in infertile women. It also increased the likelihood of spontaneous or ICSI pregnancy [7,42-44]. In modern societies, the age of becoming a parent is increasing daily. Increasing ROS due to factors such as smoking and alcohol use, improper diet rich in fat-obesity, exposure to radiation, exposure to waste UV rays, chemical agents-pesticides, and plastic waste threatens the human body. The adverse effects of OS on fertility are inevitable [6,8]. Although exposure to risk factors for ROS can be controlled in some cases, it often develops against our will. For this reason, dietary and lifestyle changes, as well as nutritional supplements with antioxidant content, are gaining importance.

In our study, daily astaxhantin (5 mg), coenzyme Q10 (100mg), L-Arginine (250mg), L-Carnitine (250mg), Selenium (100mcg), Zinc (10mg), Folic acid (400mcg), Vitamin E (100mg) and Vitamin C (100mg) antioxidant-multiprotein supplement, we found significant improvement in semen volume, sperm count, progressively motile sperm ratio, morphology and viability parameters at the end of the 4th month in infertile men. In addition, an increase in the number of motile sperm was observed. According to our other data; When compared to the group that did not take nutritional supplements, it was determined that the use of antioxidant-multiprotein complex was accompanied by increased semen volume, sperm concentration, and total and progressively motile sperm count, which was statistically significant. Our results were similar to the relevant literature.

Conclusion
It was determined that antioxidant-multiprotein-containing nutritional supplements containing Astaxhantin, coenzyme Q10, L-arginine, L-carnitine, selenium, zinc, and vitamins E and C provided significant improvement in semen volume, sperm morphology, vitality and motility. In this context, we predict that the antioxidant-multiprotein complex can be used as a food supplement for the supportive treatment of male infertility. Prospective or randomized studies should be done for getting better outcomes in this subject.

Disclosure
Authors have no potential conflicts of interest to disclose.

References