Case Reports and Reviews

Case Report

A Case Report on the Management of Combined Factor Infertility and Successful Pregnancy with Intracytoplasmic Sperm Injection and In Vitro Fertilization After Cyclofert-IVA® Pretreatment

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Abbreviations

ART: Assisted Reproduction Technology; CoQ10: Co-Enzyme Q10; DHEA: Dehydroepiandrosterone; E2: Estradiol; FSH: Follicle Stimulating Hormone; HCG: Human Chorionic Gonadotropin; ICSI: Intracytoplasmic Sperm Injection; IVF: In Vitro Fertilization; LH: Luteinizing Hormone; OAT: Oligo-Astheno-Terato-zoospermia; TSH: Thyroid Stimulating Hormone

Abstract

Background: *Infertility affects about 17% of people worldwide, with most cases attributed to female, male, or combined factors. While assisted reproductive technologies, particularly in-vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), are widely used treatment options, adjunct nutraceutical therapies such as Cyclofert-IVA® have emerged to support female reproductive health and improve factors associated with infertility.*

Case Summary: *We report the case of a 26-year-old Libyan woman presenting with a 3-year history of primary infertility and no identifiable female pathology. Her hormonal profile, pelvic imaging, and tubal patency were all within normal limits, indicating unexplained female infertility. However, the male partner was diagnosed with oligo-astheno-teratozoospermia. Given the combined factor infertility diagnosis, the couple underwent in vitro fertilization with intracytoplasmic sperm injection, following a one-month course of Cyclofert-IVA®, a combination of dehydroepiandrosterone, high dose coenzyme Q10, L-methylfolate, vitamins E and D, Ginkgo biloba, and omega-3 for the female partner. Three blastocysts were transferred, resulting in a confirmed intrauterine clinical pregnancy with positive fetal cardiac activity at 7 weeks' gestation.*

Conclusion: *A one-month Cyclofert-IVA® pretreatment before IVF/ICSI may improve fertility outcomes in couples with combined factor infertility. However, larger prospective trials are needed to confirm its efficacy and establish its role in routine infertility clinical practice.*

Introduction

According to the World Health Organization (WHO), infertility impacts about 17% of people worldwide at some point during their lives [1]. Around 85% of couples affected by infertility are diagnosed with female infertility, male infertility, or combined factors infertility, where both female and male causes co-exist. The remaining 15% of cases are labeled as having unexplained infertility [2]. An assessment of ovulatory function, ovarian reserve, uterine cavity, tubal patency, and a semen analysis are essential components of the workup for couples experiencing infertility [3]. The results from this evaluation help guide the selection of adequate treatment strategies. Assisted reproductive technologies (ART), specifically in vitro fertilization (IVF) with or without intracytoplasmic sperm injection (ICSI), are now widely applied for the treatment of infertility, particularly for cases, including endometriosis, male factor, and unexplained infertility [2].

In recent years, nontraditional, alternative treatments have been considered as adjunct therapies in the management of infertility. Oral therapies, often containing antioxidants, vitamins, minerals, fatty acids, and hormone precursors, are thought to counteract oxidative stress, improve mitochondrial function, regulate hormonal balance, and enhance gamete and endometrial quality. One such emerging formulation is Cyclofert-IVA®, a targeted nutraceutical designed to support female reproductive health. Its comprehensive formulation includes several bioactive ingredients, many of which have demonstrated potential beneficial effects on ovarian function, oocyte quality, and endometrial receptivity in women. Each capsule contains 25 mg of dehydroepiandrosterone (DHEA), a high dose of 200 mg of Coenzyme Q10 (CoQ10), 200 µg of L-methylfolate (MTHF), 200 mg of vitamin E, 1000 IU of vitamin D, 25 mg of ginkgo biloba, and 220 mg of omega-3 fatty

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acids. These components were carefully selected for their complementary roles in improving factors involved in female infertility.

Recent meta-analyses and studies suggest that the key ingredients of Cyclofert-IVA® provide reproductive benefits: DHEA has been linked to improved oocyte quality and higher pregnancy rates; CoQ10 enhances mitochondrial function and embryo quality; ginkgo biloba may improve uterine blood flow and provide antioxidant protection; omega-3 fatty acids are associated with better oocyte quality and reduced inflammation; vitamin D has been shown to support implantation and increase ovarian reserve markers, and vitamin E may reduce oxidative stress and improve endometrial thickness [4].

To date, however, no study has investigated whether this combination treatment could improve the IVF treatment outcomes in couples with combined factor infertility. Herein, we report the case of primary infertility involving combined male and female factors, which achieved a successful clinical pregnancy following one month of dietary pretreatment with Cyclofert-IVA® before an IVF/ICSI cycle.

Case presentation

Patient information

We report the case of a 26-year-old female Libyan housewife who presented with a chief complaint of primary infertility for the past 3 years, despite regular, unprotected intercourse.

Medical/Surgical history

The patient reportedly had no significant medical or surgical history. Gynecological history was unremarkable with regular menstrual cycles and no history of pelvic inflammatory disease, endometriosis, or thyroid disorders. A previous basic fertility evaluation and hormonal reports were within normal limits, indicating no medical issues that could lead to infertility. The patient also reported a healthy lifestyle, with no tobacco use, alcohol consumption, or exposure to drugs. The male partner's overall health was satisfactory; however, a prior semen analysis indicated poor semen parameters.

Physical examination

Upon physical examination, the patient appeared well-nourished and well-developed, showing no signs of acute distress. Her body mass index was calculated to be 23.4 kg/m², which falls within the normal weight range. Her vital signs included a blood pressure of 118/76 mmHg, indicating a normotensive state, a temperature of 36.8°C, a heart rate of 76 beats per minute, and a respiratory rate of 16 breaths per minute.

Abdominal examination revealed a normal soft abdomen with no masses or tenderness. Bimanual pelvic examination revealed normal external genitalia, a healthy cervix, and a normal-sized uterus in an anteverted position, with no adnexal masses or tenderness.

Diagnostic assessment

The patient was advised to undergo blood examinations on the third day of her menstrual cycle to evaluate a complete hormonal profile, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), prolactin, and thyroid-stimulating hormone (TSH). The results, presented in Table 1 along with the reference ranges, were normal for the patient's reproductive age.

Table 1. *Cycle day three hormonal profile of the patient.*

Hormones	Clinical findings	Reference ranges[5]
FSH, mIU/mL	6.8	3.3 – 9.5
LH, mIU/mL	5.1	< 7.0
E2, pg/mL	45.0	25.0 – 75.0
Prolactin, ng/mL	12.0	< 24.0
TSH, µIU/mL	1.8	0.4 – 4.0
FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, E2: Estradiol, TSH: Thyroid-stimulating hormone.		

Transvaginal ultrasonography performed on the third day of the menstrual cycle showed normal uterine morphology and two normal-sized ovaries, with no ovarian cysts. A trilaminar endometrial morphologic pattern was also observed, with a thickness of 7 mm. All follicles between 2 and 10 mm observed in both ovaries were counted, and the antral follicle count was found to be 16, which was within the reference range for healthy women (a total of 5-17 follicles) [6]. Hysterosalpingography, also prescribed as part of the female infertility workup, showed normal morphology and contours of the uterine cavity, as well as normal tube spillage into the abdominal cavity, suggesting bilateral patent fallopian tubes.

The male partner was advised to undergo semen analysis, and the sample of semen was collected in the laboratory. Patient seminal parameters were obtained and are presented in Table 2. The volume of semen measured 3 mL, falling within the acceptable range; however, the sperm concentration, total motility, and morphology were notably lower than the reference value. Thus, the partner was diagnosed with oligo-astheno-terato-zoospermia, referred to as OAT. OAT is defined as a disturbance of three semen parameters, denoting decreased sperm concentration (oligo-zoospermia), abnormal sperm motility (astheno-zoospermia), and impaired sperm morphology (terato-zoospermia) [8].

Based on normal ovulatory function, tubal patency, and uterine anatomy with no identifiable female pathology, along with the male partner's diagnosis of OAT, a combined factor infertility diagnosis was established: male factor infertility and female unexplained infertility.

Table 2. *Semen analysis of the male partner.*

Semen Parameters	Clinical findings	Reference ranges according to WHO[7]
Volume of semen, mL	3.0	≥1.4 mL
Sperm concentration, million/mL	12.0	≥39 million/ml
Total sperm motility (PR + NP), %	28.0	≥42%
Sperm morphology (normal forms), %	3.0	≥4%
PR: Progressive motility, NP: Non-progressive motility.		

Interventions

This case of combined factor infertility required the use of IVF with ICSI as a first-choice therapy, and the couple was counseled regarding the need for ICSI treatment, given the quality of sperm. As an adjuvant therapy, the female patient was prescribed Cyclofert-IVA®, a combination of DHEA, high dose CoQ10, MTHF, vitamins E and D, Ginkgo biloba, and omega-3 fatty acids. Both individuals provided informed consent before proceeding with any further interventions.

The supplementation regimen was initiated one month before the ovarian stimulation protocol, consisting of one capsule of Cyclofert-IVA®, taken orally twice daily. The patient reported full adherence to the supplement with no reported adverse effects. Upon completion of the prescribed regimen, the couple underwent a full IVF/ICSI cycle following the standard protocol, including controlled ovarian hyperstimulation with gonadotropins, triggering with human chorionic gonadotropin (hCG), transvaginal oocyte retrieval, fertilization via ICSI using the partner's sperm, embryo culture, and subsequent transfer of three viable blastocysts.

Follow-up and outcomes

The patient was monitored throughout the stimulation phase with multiple ultrasounds and hormonal assays, which showed an adequate response; subsequently, the embryo transfer was performed without complications. A follow-up appointment was scheduled on day 14, during which the patient underwent a serum β-hCG test. The test yielded a positive result with a reading of 350 mIU/mL, confirming a biochemical pregnancy. A follow-up ultrasound at 7 weeks of gestation confirmed an intrauterine gestational sac with a fetal pole and positive cardiac activity, confirming a clinical pregnancy.

Discussion

The present report describes a case of a successful pregnancy outcome of a female with unexplained infertility and comorbid male factor infertility, with the administration of Cyclofert-IVA® for one month before an IVF/ICSI cycle.

One of the most probable explanations for the successful IVF outcome in this case is the improvement of oocyte quality through Cyclofert-IVA® supplementation. Its formulation, which includes mostly DHEA and CoQ10, can not only enhance folliculogenesis and mitochondrial function but also reduce oxidative stress. These effects thereby support the development of high-quality oocytes capable of sustaining healthy fertilization and normal embryo growth. Meta-analyses and systematic reviews suggest that DHEA supplementation in women of advanced age or with poor ovarian response may improve oocyte quality and consequently IVF outcomes and pregnancy rates [9–11]. Similar positive effects on oocyte quality and pregnancy rates were reported in infertile women undergoing ART and treated with CoQ10 either alone [12,13] or in combination with DHEA [14,15], as evidenced by recent meta-analyses and systematic reviews. Additionally, studies showed that supplementation with vitamin E [16] and omega-3 fatty acids [4,17,18] has been shown to protect oocytes from oxidative damage and enhance their membrane integrity in infertile women. In our case, this combination in Cyclofert-IVA® likely contributed to improved oocyte quality and subsequently to the development of a good-quality embryo, despite severe male factor infertility. Studies have shown that high-quality oocytes are capable of repairing sperm DNA damage, particularly if the damage is minor [19,20], which may explain the favorable embryonic development observed in our patient.

Embryo implantation and successful pregnancy require not only a high-quality, well-developed embryo but also an adequately receptive endometrium. In our case, another important consideration is the potential improvement in endometrial receptivity following Cyclofert-IVA® treatment. The current evidence from meta-analyses and systematic reviews demonstrates that DHEA and vitamin E supplementation significantly increase endometrial thickness and improve IVF/ICSI outcomes, thereby enhancing the clinical pregnancy rate [16,21,22]. Gingko biloba, through its vasoregulatory effects, was found to improve endometrial thickness by increasing uterine blood flow in women with a history of failed IVF/ICSI cycles [22]. Furthermore, MTHF, the bioactive form of folate present in Cyclofert-IVA®, may also have contributed to enhanced endometrial receptivity by lowering homocysteine levels, which have been negatively associated with implantation and clinical pregnancy in patients with a history of IVF/ICSI failure [23]. Vitamin D supplementation was shown to be effective in improving the clinical pregnancy rates of infertile women undergoing ART, by enhancing embryo implantation and the decidualization of the endometrium [24]. Finally, omega-3 fatty acids may have complemented these effects in supporting a receptive endometrium by reducing oxidative stress and inflammation of the endometrium, which positively impacts implantation [25].

Our observations from this case study underscore the potential benefits of this combination, specifically through the synergistic effects of its ingredients, which may have contributed to higher oocyte quality and endometrial competence, thus maximizing the chances of successful implantation and pregnancy. It is also worth mentioning that the intervention in this study consisted of total daily doses of 50 mg of DHEA and 400 mg of CoQ10 for one month only, prior to the ovarian stimulation protocols. This represents higher doses than those used in other interventions, and considerably shorter treatment duration. For instance, the optimal treatment regimen for CoQ10 is 30 mg per day for 3 months before the controlled ovarian stimulation cycle [26], and 75 mg per day for 8 to 12 weeks for DHEA [21]. Despite this short course, our patient achieved positive IVF outcomes and sustained pregnancy, which further highlights the benefits of Cyclofert-IVA® as an effective and fast-acting combination to optimize IVF-ICSI outcomes.

Although the current evidence suggests a positive impact of Cyclofert-IVA® supplementation on various infertility factors related to oocyte quality, endometrial receptivity, and implantation, further well-designed, large-scale randomized controlled trials are necessary to validate these findings and conclusively establish the efficacy of Cyclofert-IVA® as an adjunct treatment in IVF protocols for infertility involving unexplained female factor or combined factors.

Conclusion

A one-month pretreatment course with Cyclofert-IVA® administered before undergoing an IVF-ICSI cycle seems to have potential benefits in achieving positive IVF/ICSI outcomes in a patient with unexplained infertility and a comorbid male factor. While supplementation worked well alongside standard IVF in a single case, more extensive and prospective trials are necessary to prove Cyclofert-IVA®'s efficacy in improving IVF/ICSI outcomes and maximize its integration into clinical practice as part of a comprehensive approach to treating couples with combined factor infertility.

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