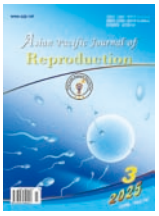

Original Article

Asian Pacific Journal of Reproduction

Journal homepage: https://journals.lww.com/apjr/

doi: 10.4103/apjr.apjr_233_24

# Effect of two doses of coenzyme Q10 on spermogram parameters, sperm chromatin integrity and partner pregnancy rate in men with idiopathic oligoasthenozoospermia: A prospective study

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## ABSTRACT

**Objective:** To evaluate the effectiveness of two doses of coenzyme Q10 (CoQ10) on semen parameters, sperm DNA damage, and the partner pregnancy rate in men with idiopathic oligoasthenozoospermia.

**Methods:** 250 patients with idiopathic oligoasthenozoospermia were examined. The first group ($n$=125) received 100 mg/day of CoQ10 and the second group ($n$=125) received 200 mg/day of CoQ10 orally for 6 months. Semen parameters, DNA fragmentation index (DFI) and the partner pregnancy rate were analyzed at baseline and after 6 months of treatment.

**Results:** Comparing with baseline data, treatment with CoQ10 (100 mg/day or 200 mg/day) resulted in a significant increase in sperm concentration (both $P$<0.001), a significant improvement in progressive motility and total motile sperm count ($P$=0.05, $P$=0.001, respectively). The mean DFI was significantly improved after treatment with CoQ10 at 100 mg/day and at 200 mg/day, after 6 months of treatment ($P$<0.01). Moreover, CoQ10 significantly improved the partner pregnancy rate. A strongest correlation was found between seminal fluid parameters and DFI ($P$<0.001).

**Conclusions:** CoQ10 is effective in improving semen parameters, DFI and on the partner pregnancy rate after 6 months with CoQ10 at two doses, with a greater improvement shown in men who took 200 mg/day than in those who took 100 mg/day.

**KEYWORDS:** Antioxidants; Coenzyme Q10; Oxidative stress; Idiopathic oligoasthenozoospermia; Male infertility

## 1. Introduction

Infertility is defined as the inability to achieve successful pregnancy after 12 months of regular unprotected sex[1]. The prevalence of infertility has increased significantly in recent decades, and it has been estimated that approximately 15% of reproductive-age couples suffer from infertility, which has become a global concern[2]. Sperm quality remains, of course, the determinant of male fertility, and standardized sperm analyses consist of a descriptive analysis of sperm parameters[3]. New parameters are

### Key Points

**Question:** What is the effect of two doses of oral coenzyme Q10 (CoQ10) supplementation, as an antioxidant, on male fertility?

**Results:** The study demonstrated the beneficial effect of CoQ10 as a first-choice dietary supplement for the treatment of male infertility and the improvement of endocrine disturbances in men suffering from idiopathic male infertility, and subsequently a high procreation rate in couples with male infertility.

**Meaning:** CoQ10 is effective in improving semen parameters, DNA fragmentation index and the partner pregnancy rate, at 200 mg/day.

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**How to cite this article:** Rochdi C, Adli O, Taheri H, Saadi H, Mimouni A, Choukri M. Effect of two doses of coenzyme Q10 on spermogram parameters, sperm chromatin integrity and partner pregnancy rate in men with idiopathic oligoasthenozoospermia: A prospective study. *Asian Pac J Reprod* 2025; 14(3): 114-121.

**Article history:** Received: 23 December 2024; Revision: 10 March 2025; Accepted: 15 April 2025; Available online: 10 June 2025

increasingly invested in the evaluation of sperm quality, such as the integrity of the sperm nucleus, particularly through the measurement of the degree of DNA fragmentation, as well as the degree of spermatic oxidative stress[4]. Male infertility can be linked to several factors, including environmental factors, infection, genetic, endocrine, varicocele, cryptorchidism, autoimmune diseases, systemic diseases, and testicular cancer[5,6]. Nevertheless, in 30% to 40% of patients, no underlying cause of infertility is identified, under the term of idiopathic male infertility, related to an alteration of one or more sperm parameters[1]. Idiopathic oligoasthenozoospermia includes a combination of low sperm concentration ($<16\times10^6$/mL), and reduced motility (progressive motility <30% and total motility <42%) by the 6th edition of World Health Organization guidelines (2021) in men who do not have any disease that could affect their fertility[7]. Several mechanisms have been suggested to explore idiopathic male infertility, including analysis of conventional sperm parameters, sperm DNA fragmentation, assay of biochemical and oxidative stress (OS) markers[8]. OS is the result of an imbalance between pro-oxidants and antioxidant defense mechanisms, which causes in a state of redox paradox, which leads to DNA damage, peroxidation of plasma membrane lipids, and protein oxidation[9,10]. Reactive oxygen species (ROS) are essential to regulate sperm physiological processes required for male reproduction such as capacitation and acrosome reaction[11]. However, high levels of ROS are detrimental to sperm, as sperm have limited intrinsic antioxidant capacity[12]. Excessive production of ROS has been correlated with a reduction of sperm motility, sperm DNA damage, abnormal embryonic development, increased anomalies of sperm morphology, resulting in male infertility and negatively affecting reproductive outcomes[13]. Furthermore, high levels of ROS were detected in semen samples in 25% to 40% of infertile men[14]. OS could be caused by endogenous factors such as immature sperm, metabolic processes, and leukocytes, as well as exogenous factors such as infection, environmental toxins, smoking, alcohol, obesity, varicocele, malignancy, radiotherapy, chemotherapy, and systemic disease[12]. Spermatozoa have a limited intrinsic antioxidant capacity and DNA repair system[15]. Fortunately, the seminal fluid contains a set of antioxidants that protect spermatozoa against OS and that allow maintenance of the balance between reduction and oxidation, including non-enzymatic antioxidants such as vitamins A, C, and E, coenzyme Q10 (CoQ10), *L*-carnitine, glutathione, carotenoids, zinc, and selenium, as well as enzymatic components, such as catalase, glutathione peroxidase (GPx), and superoxide dismutase (SOD)[16,17]. The implementation of treatment with supplementation of oral antioxidants in order to improve idiopathic male infertility, is a procedure that is now widely adopted by researchers and clinicians, and is the subject of a relatively small number of publications, particularly in Morocco[18]. Various oral antioxidants have been the subject of intensive research in recent years[16]. CoQ10 is a fat-soluble ubiquinone, as a dietary, nutraceutical supplement, and a potent antioxidant that protects sperm against ROS-induced damage[19]. It plays a critical role in both cellular energy metabolism at the mitochondrial level and preventing lipid peroxidation of sperm cell membranes. The protective effects of supplemental CoQ10 on sperm have been amply documented[20].

CoQ10, non-enzymatic antioxidant, has been also reported to improve semen parameters in several studies. In a recent study, exogenous administration of CoQ10 was effective for improving sperm parameters in patients with idiopathic asthenozoospermia[21]. Furthermore, an open-label prospective study found that CoQ10 supplementation improved semen quality with beneficial effects on pregnancy rate[22]. Our previous study showed improvement of semen parameters, reproductive hormones and sperm DNA fragmentation in infertile men with idiopathic oligoasthenotertaospermic after supplementation of oral antioxidants with CoQ10[23]. Treatment with CoQ10 may improve seminal fluid parameters, live births, and clinical pregnancy rates, but there is lack of agreement on the type of antioxidant, dose, and duration of treatment. Therefore, the present study aims to evaluate the effect of oral CoQ10 treatment at doses of 100 mg/day or 200 mg/day for 6 months on conventional sperm parameters, sperm DNA damage, and spontaneous pregnancy rates after treatment in infertile men with idiopathic oligoasthenozoospermia.

## 2. Methods

### *2.1. Patient recruitment*

Among the 268 patients initially selected in the study to start this prospective study, 250 patients [mean age: (29.9±3.6) years)] with idiopathic oligoasthenozoospermia were recruited at Reproductive Center, Andrology Laboratory, Mohammed VI University Hospital Center in Oujda, Morocco, between June 2022 and September 2023. The sample size of our study was collected based on the number of patients who had undergone the CoQ10 treatment prescribed at our fertility center and who had agreed to participate in the study by providing information from their semen analysis. All patients underwent a medical assessment including physical examination, and laboratory and radiological investigations.

The inclusion criteria comprised a history of infertility of at least 1 year despite regular unprotected intercourse. Oligoasthenozoospermia was defined according to the sixth edition of the World Health Organization (WHO) 2021 criteria (concentration $<16\times10^6$/mL, motility ≤42%, progressive motility ≤30%, morphology >4%). Subjects taking CoQ10 treatment during last 6 months were included in this study.

Exclusion criteria were: men with varicocele; genital infection;

cryptorchidism; azoospermia; testicular trauma or scrotal surgery; smoking and endocrine systemic illnesses.

There was no apparent female factor, since all partners [(26.0±1.1) years; range 21–34 years] were ovulating regularly as formally proven by luteal phase progesterone levels and no abnormal fallopian tube anatomy was detected after hysterosalpingography.

The study was conducted as a prospective study. Selected patients who meet the selected selection criteria were divided into two treatment groups. Group 1 ($n$=125) received 100 mg (single dose) of oral CoQ10 and group 2 ($n$=125) received 200 mg (single dose of 100 mg) of oral CoQ10, daily for 6 months. The lifestyle factors were minimized: nutritional (red meat and saturated fats), physical (excessive heat exposure) and chemical (smoking, alcohol, drugs and pollutants). Semen analysis, DNA integrity, number of motile spermatozoa inseminated and pregnancy rate were measured in semen samples and compared before and after therapy with CoQ10.

The marketed drug, CoQ10, used as an antioxidant therapy in the treatment of male infertility, contains 100 mg of CoQ10 per tablet. Patients in one group were prescribed one tablet per day, equivalent to 100 mg, while the other group received two tablets per day, equivalent to 200 mg/day. The duration of treatment, which is 6 months, depends on the degree of improvement. In fact, it was noted that after 3 months of treatment, there was little improvement compared to 6 months of treatment, hence the choice of this treatment duration.

After six months of treatment with two doses of CoQ10, a semen sample was delivered before and after treatment, respecting the same abstinence time as for the initial semen sample (before treatment). The outcome was to compare the effect of two doses of CoQ10 (100 and 200 mg) on conventional semen parameters, DNA integrity and pregnancy rate (spontaneous, intra-uterine insemination). Other outcomes were to investigate a possible correlation between spermatic parameters [concentration, progressive motility, total motile sperm count (TMSC)] and DNA fragmentation index (DFI) in recruited patients.

### 2.2. Semen analysis

Samples were analyzed and classified according to the 2021 WHO guidelines for examination and processing of human semen[7]. A clean sterile plastic container confirmed to be non-toxic for spermatozoa was given to each participant to produce semen samples by masturbation (after 2-3 days of sexual abstinence). All semen analyses were performed by the same technician for data consistency, and all patients underwent two semen analyses before and after treatment with CoQ10, and mean values were calculated.

To minimize temperature fluctuations and control the time between semen sample collection and analysis, samples were collected in our Unit. Macroscopic analysis of the sperm was performed after liquefaction at 37℃. The evaluation of concentration and motility of spermatozoa parameters was conducted using the Computer Assisted Sperm Analyzer (SCA, MICROPTIC, Barcelona, Spain). For each measurement, a 2.5 μL aliquot of sperm was loaded into a standard four-chamber slide (Leja, NL, Nieuw-Vennep the Netherlands). The spermatozoa with fast and slow progressive motility were counted (grade A+B), followed by the non-progressive motile (grade C) and non-motile spermatozoa (grade D). Sperm concentration count and sperm motility were determined using ×10 magnifications. The evaluation of the spermatozoon morphology was made based on Modified David criteria and was evaluated using the the Diff-Quik kit (Dade Behring AG, Dudingen, Switzerland), and more than 200 sperms were observed *via* microscope (Nikon eclipse e200).

### 2.3. Total motile sperm count analysis

Using a two-layered density gradient centrifugation technique, sperm samples were prepared (50% and 90% Isolate, Irvine Scientific, Santa Ana, USA). Male-factor infertility was not strictly defined but rather was assessed by analyzing the number of motile sperm in the ejaculate. TMSC in the ejaculate was calculated using the formula: TMSC = semen volume (mL) × sperm concentration (millions per mL) × percentage motility divided by 100 (percentage). In addition, the patients was further divided into 4 groups according to the total motile sperm count based on the WHO reference as less than $0.5\times10^6$; $0.5\times10^6$-$1\times10^6$; $1\times10^6$-$2\times10^6$ and greater than $2\times10^6$.

### 2.4. DNA integrity assessment

DNA fragmentation index was evaluated in patients after 2, 4, and 6 months of treatment of CoQ10 with 2 doses, 100 mg/day and 200 mg/day.

DNA fragmentation was assessed by Sperm Dispersion Chromatin test (SCD) and with protocol validated in our previous study[10]. In the absence of massive sperm DNA breakage and following acid denaturation and removal of nuclear proteins, dispersed DNA loops produce a characteristic halo. Sperm with fragmented DNA does not develop such a halo, or it is small. DNA fragmentation test was performed using the sperm dispersion chromatin method by Spermfunc® DNA kit at BRED Life Science Technology Inc., China. The agarose was placed at a temperature of 90℃-100℃ for 20 min and heated at 37℃ for 5 min. Then, the semen was added to the agarose and mixed well. The suspension was poured on agarose-coated slides and covered with a 20 mm × 20 mm cover glass. The slides cooled at 4℃ for 5 min, and then were slowly opened. They were then incubated in a denatured solution at 22℃ for 7 min and with lysis solution at room temperature for 25 min. After washing with $H_2O$ for 5 min, they were dehydrated with graded ethanol at 70%, 90%, and 100% for 2 min per concentration. The slides were dried and stained with Wright's solution for 25 min. This is followed by observation *via* a light microscope based on various halo images,

namely large, medium, and small, no halo, and degraded sperms. Normal spermatic DNA presented radiate halos and damaged spermatic DNA presented no or small halos. Fragmented sperm referred to those having a small or no halo. The thickness of the halo on one side was less than the 1/3 diameter of the head's thinnest part. A minimum of 500 sperm were counted on each sample under the 100× magnification.

The rate of sperm DNA fragmentation: DFI (%) = (Number of spermatozoa with fragmented DNA/Total number of spermatozoa) × 100, and <25% was considered normal.

### 2.5. Pregnancy rate

The pregnancy rate of couples was evaluated after 6 months of treatments with CoQ10 at 2 doses (100 and 200 mg) in patients with oligoasthenozoospermia. The assessment of spontaneous pregnancies following ovarian stimulation performed by gynecologists on women, combined with intrauterine insemination (IUI)—a procedure involving the placement of laboratory-treated sperm into the uterus—provides insights into fertility outcomes.

### 2.6. Statistical analysis

Statistical analysis was performed using SPSS software ver. 24 (IBM Corp., Armonk, NY, USA). Normality of data was assessed by Kolmogorov–Smirnov test. Paired Student's *t*-test was used to compare means before and after CoQ10 administration. The data were expressed as mean±standard deviation (mean±SD). Correlations between sperm parameters and DNA integrity were analyzed using the Pearson correlation coefficient (*r*). For all tests, a *P*-value lower than 0.05 was considered to indicate statistical significance.

### 2.7. Ethics statement

This study was approved by the the Research Ethical Review Committee of Faculty of Medicine and Pharmacy of Oujda, Morocco (Approval code: 02/2023; approval date was 4 April 2023). The participants were informed of the scientific nature of our study.

## 3. Results

### 3.1. Effect of CoQ10 supplementation on spermatic parameters

A total of 250 patients were included in the study, with 125 patients in group 1 and 125 patients in group 2. The mean age was (30.7±4.5) years and (29.1±2.6) years in groups 1 and 2, respectively, and the mean duration of infertility was (5.2±2.1) years and (4.9±1.2) years in groups 1 and 2, respectively (Table 1).

Their spouse's mean age was (30.1±2.7) years in group 1 and (29.2±3.8) years in group 2. 6 months of CoQ10 therapy (100 mg or 200 mg per day) resulted in a significant increase in sperm concentration ($P$=0.002, $P$<0.001, respectively), as well as improvements in progressive motility ($P$<0.001, $P$<0.001, respectively), and a significant improvement in total motility ($P$<0.001, $P$<0.001, respectively). These changes were better in the group treated with 200 mg of CoQ10 (Table 1).

Likewise, treatment with CoQ10 (100 mg/day or 200 mg/day) resulted in significant increases in total motile sperm count ($P$=0.021, $P$<0.001, respectively), with greater changes in subjects treated with 200 mg of CoQ10 (Table 1).

### 3.2. Effect of CoQ10 supplementation on DFI

Treatment with CoQ10 resulted in significant decreases in sperm DFI. The mean of DFI after treatment with CoQ10 at 100 mg/day was significantly improved after 2, 4, and 6 months of treatment ($P$<0.05). In addition, the mean of DFI after treatment with CoQ10 at 200 mg/day was significantly improved after 2, 4, and 6 months of treatment ($P$<0.05) (Table 2).

Moreover, in group 1 (100 mg/day), significant positive correlations were found between sperm concentration and DFI ($r$=0.22, $P$=0.005), total motility ($r$=0.15, $P$=0.010), morphology ($r$=0.75, $P$=0.026), and TMSC ($r$=0.47, $P$=0.002). Furthermore, in group 2 (200 mg/day), similar correlations were between sperm concentration and

**Table 1.** Participants' characteristics and semen parameters before and after CoQ10 treatment.

| Parameters | CoQ10 100 mg/day ($n$=125) | | $P$-value | CoQ10 200 mg/day ($n$=125) | | $P$-value |
|---|---|---|---|---|---|---|
| | Before | After | | Before | After | |
| Age, years | 30.7±4.5 | 30.7±4.5 | | 29.1±2.6 | 29.1±2.6 | |
| Duration of infertility, years | 5.2±2.1 | 5.2±2.1 | | 4.9±1.2 | 4.9±1.2 | |
| Sperm volume, mL | 2.34±0.42 | 2.63±0.29 | 0.086 | 2.39±0.42 | 2.77±0.42 | 0.060 |
| Sperm concentration, M/mL | 8.78±1.40 | 12.39±2.08 | 0.002 | 9.17±0.93 | 13.09±1.87 | <0.001 |
| Total sperm count, M/ejaculate | 20.39±4.05 | 32.66±6.96 | 0.001 | 21.73±3.27 | 36.00±5.92 | <0.001 |
| Progressive mobility (a+b), % | 20.36±1.24 | 28.83±1.83 | <0.001 | 21.60±1.34 | 31.66±1.26 | <0.001 |
| Total motility (a+b+c), % | 30.15±1.02 | 37.67±1.91 | <0.001 | 31.53±1.35 | 42.58±2.03 | <0.001 |
| Live spermatozoa, % | 38.70±1.34 | 44.30±1.89 | <0.001 | 44.44±4.79 | 54.30±4.57 | <0.001 |
| Normal strict forms, % | 8.96±0.99 | 11.78±1.34 | <0.001 | 10.07±1.41 | 14.84±0.78 | <0.001 |
| Total motile sperm count, Million | 1.05±0.16 | 1.49±0.31 | 0.021 | 1.06±0.15 | 1.68±0.55 | <0.001 |

Data are expressed as mean±SD. M: Million, $\times 10^6$ spermatozoa; CoQ10: coenzyme Q10. a+b: the spermatozoa with fast and slow progressive motility, c: non-progressive motile.

**Table 2.** Sperm DNA fragmentation index (DFI) before and after 2, 4 and 6 months of CoQ10 treatment.

| Groups | DFI before treatment (%) | DFI after treatment (%) | | | *P*-value |
|---|---|---|---|---|---|
| | | 2 months | 4 months | 6 months | |
| CoQ10 100 mg/day (*n*=125) | 21.60±1.14 | 21.00±1.00 | 20.50±0.71 | 18.40±1.14 | 0.008 |
| CoQ10 200 mg/day (*n*=125) | 22.60±1.14 | 20.40±0.55 | 19.00±1.00 | 16.80±2.59 | 0.002 |

Values are presented as mean±SD; CoQ10: coenzyme Q10.

**Table 3.** Correlations between semen parameters and sperm DNA fragmentation index (DFI) in patients after CoQ10 treatment.

| Variables | DFI in the group of CoQ10 100 mg/day (%) | | DFI in the group of CoQ10 200 mg/day (%) | |
|---|---|---|---|---|
| | *r* | *P*-value | *r* | *P*-value |
| Concentration | 0.22 | 0.005 | 0.75 | 0.030 |
| Total motility | 0.15 | 0.010 | 0.21 | 0.015 |
| Morphology | 0.75 | 0.026 | 0.41 | 0.020 |
| Total motile sperm count (TMSC) | 0.47 | 0.002 | 0.25 | 0.001 |

*r*: Pearson correlation coefficient. CoQ10: coenzyme Q10.

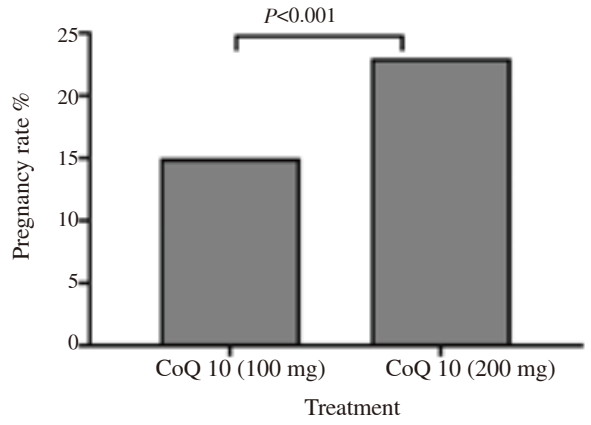


**Figure 1.** Partner pregnancy rate in 250 patients treated with CoQ10 (100 mg/day or 200 mg/day). CoQ10: coenzyme Q10.

DFI (*r*=0.75, *P*=0.030), total motility (*r*=0.21, *P*=0.015), morphology (*r*=0.41, *P*=0.020), and TMSC (*r*=0.25, *P*=0.001) (Table 3). The strongest correlations were found between sperm concentration, motility, morphology, total motile sperm count and DFI.

### *3.3. Effect of CoQ10 supplementation on partner pregnancy rate*

The treatment with CoQ10 at 100 mg/day and 200 mg/day resulted in increase in semen parameters and was reflected in the partner pregnancy rates. In group 1, for patients treated with CoQ10 at 100 mg/day, the percentage of pregnancy was 15%. However, for patients treated with CoQ10 at 200 mg/day, the pregnancy rate was increased in 23% (*P*<0.001), using assisted reproductive technology (intra-uterine insemination) (Figure 1).

## 4. Discussion

The present study demonstrated that the exogenous administration of CoQ10 exerted beneficial effects on sperm concentration, motility, sperm DNA integrity and partner pregnancy rate in men with idiopathic oligoasthenozoospermia. A dose of 200 mg/day of CoQ10 produced greater changes among patients with idiopathic male infertility. The presenet study aimed to compare the effect of two doses of CoQ10 on conventional sperm parameters, DNA integrity and spontaneous pregnancy rate after 6 months of treatment. Exogenous intake of CoQ10 may improve sperm parameters and seminal plasma antioxidant capacity[24]. Treatment with CoQ10 (200 mg twice a day) in 65 patients for 6 months improved sperm motility and morphology in patients with idiopathic oligoasthenoter atozoospermia[25]. Moreover, men with idiopathic asthenospermia that was randomized and placebo-controlled found that CoQ10 (200 mg daily) was effective in improving all seminal parameters and increasing CoQ10 levels in seminal plasma[21]. Similar findings were indicated by Safarinejad *et al* after supplementation of CoQ10 at 200 mg and at 300 mg for 26 weeks daily in men with oligoasthenoteratozoospermia[26]. According to Balercia *et al*, CoQ10 levels in seminal plasma grew higher and sperm parameters were improved after taking CoQ10 (200 mg/day) for 6 months[27]. The proper functioning of spermatozoa is dependent on adequate levels of CoQ10 due to its role in the mitochondrial respiratory chain and antioxidant properties. Mitochondrial dysfunction in spermatozoa has been associated with increased sperm DNA fragmentation, reduced sperm motility and damage to the sperm cell membrane, and reduced fertility caused by ROS[28]. OS induced structural damage of DNA, and cell death may be associated with decreased sperm count and motility[29]. In light of this, we decided to evaluate the effect of the reduced form of CoQ10 with 2 doses usually used in literature and by clinician, 100 mg/day or 200 mg/day (2 tablets of 100 mg/day), on conventional sperm parameters, chromatin integrity and therefore pregnancy rate after 6 months of treatment, equivalent of 2 cycles of spermatogenesis. Consequently, the antioxidant abilities of CoQ10 result in a decrease in OS and a boost in mitochondrial reduction-oxidation function[19]. A search in literature has demonstrated beneficial effects of CoQ10 in individual or combined form with other antioxidants on semen

parameters and pregnancy outcomes[23]. Nevertheless, there is no consensus on the type, the dose, duration of therapy, and usage of individual or combination antioxidant therapy. A recent meta-analysis showed that the doses of CoQ10 used by clinicians to treat male infertility ranged from 200 to 300 mg/day[30].

In the present study, after treatment with CoQ10 at a dose of 200 mg/day for 6 months, a significant improvement in sperm parameters was observed and had a positive effect on the procreation rate. In fact, CoQ10 is a cofactor, and its reduced form (ubiquinol) has antioxidant mitochondrial bioenergetics properties and plays a crucial role in energy metabolism and as liposoluble chain-breaking antioxidants for cell membranes and lipoproteins[20]. Ubiquinol levels are associated with cardiovascular diseases, diabetes mellitus, testicular cancer, and seminal CoQ10 levels are reduced in infertile men, which correlates with sperm parameters in particular concentration and progressive motility[31]. Numerous studies have examined the influence of CoQ10 on infertility and some of them showed that CoQ10 treatment improves semen measures and seminal antioxidant status in patients with idiopathic male infertility[24]. A strong correlation among sperm count, motility and ubiquinol-10 content in seminal fluid has been reported[32]. In addition, our study has shown that CoQ10 has a beneficial effect on sperm motility and should be administered longer than 6 months[33]. Nadjarzadeh *et al* reported a reduction in the sperm OS markers after treatment with CoQ10[34]. Antioxidant treatment reduced form of CoQ10 may improve conventional seminal parameters, live births, and clinical pregnancy rates, but there is lack of agreement on the conevenable dose, and duration of treatment and whether to use monotherapy or combination with other antioxidants. In a double-blind placebo-controlled, and randomized study, CoQ10 administration at 300 mg/day significantly improved three semen parameters (density, motility, and morphology)[21].

Furthermore, in our previous study, administration with multiantioxydants with CoQ10 significantly improved the semen quality (concentration, motility, DFI)[23]. Moreover, a study show that after 6 months therapy with CoQ10, the sperm motility was improved and twelve spontaneous pregnancies were occurred[24]. In the light of the result of our study, and other studies on the beneficial effect of CoQ10, this therapy based on CoQ10, is affordable, safe, and easy to administer once the optimal effective dose is determined. However, overdosing on antioxidants can lead to a shift in the reduction-oxidation balance to reductive stress, which is just as damaging as OS[35].

In our study, we also observed improvements in sperm parameters especially concentration, progressive mobility, and a reduction in the rate of DNA fragmentation of spermatozoids and subsequently a significant reproduction rate after treatment with CoQ10 during 2 cycles of spermatogenesis (6 months), as well as positive correlations between the DFI and sperm parameters. Our results are correlated with previous reports detected that treatment with antioxidants is in fact associated with improved sperm DNA integrity and with an increased pregnancy rate[36]. Indeed, sperm DNA fragmentation is irreversible and leads to alteration of sperm function, resulting in infertility and excessive sperm DNA damage has been shown to compromise male fertility[37,38]. However, studies of the effects of CoQ10 intake on sperm DNA damage and pregnancy rate are limited. Our results are consistent with those of Nadjarzadeh *et al*, who showed that the administration of CoQ10 (200 mg/day for 3 months) improves the seminal parameters of infertile men[34]. Therefore, a positive correlation was found between seminal CoQ10 level and semen parameters.

In addition, CoQ10 is believed to block proinflammatory signals by insulin, interleukin-17, and signal transducer and activator of transcription 3 (STAT3), as well as tumor necrosis factor alpha and different chemokines. CoQ10 is typically concentrated in the mitochondria for use in energy-dependent process such as sperm movement, and also modulates gene expression, cell signaling, transport, and metabolism[38–40]. Future research is necessary to understand the mechanisms behind the enhancement of antioxidant capacity by CoQ10. Our research team is deepening and launching randomized studies on the effect of CoQ10 therapy on several profiles of patients with male infertility, including the profile of patients with varicocele at different grades. We did not examine the antioxidant status of patients by the determination of OS markers after therapy, because researcher Ahmed Alahmar has already reported these markers on his scientific paper. Limitations of this study is showed, including the lack of long-term follow-up, and was to provide a sufficient quantity of medication to patients with low social status.

In conclusion, treatment with CoQ10 improved sperm motility, concentration, and level of sperm DNA damage and a remarquable spontaneous pregnancy rate in infertile men with idiopathic oligoasthenozoospermia, with a greater improvement observed in response to a dose of 200 mg/day than a dose of 100 mg/day. CoQ10 therapy for 6 months can enhance the fertility potential and reproductive outcomes of men with idiopathic infertility.

## Conflict of interest statement

The authors have no competing interests to declare.

## Acknowledgements

We would like to thank all the collaborators and teams of the assisted human reproduction unit who authorized and facilitated the data's collection.

## Funding

This study receives no extramural funding.

## Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

## Authors' contributions

Chaymae Rochdi contributed to concept, acquisition, writing-original draft, methodology, validation, visualization, writing-review & editing, formal analysis, and ressources. Othmane Adli performed methodology, validation, and software. Hafsa Taheri contributed to investigation, acquisition, methodology, and validation. Hanane Saadi contributed to validation, writing-review & editing, formal analysis, and supervision. Ahmed Mimouni contributed to validation, project administration, data curation, supervision, and resources. Mohammed Choukri contributed to writing-review & editing, project administration, data curation, supervision, and resources. All authors have read and approved the final version of the manuscript.

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Edited by Lin LY, Lei Y