

# Restoring Male Fertility Impaired by Heavy Metal Exposure: A Study on the Effectiveness of a Combined Antioxidant Supplementation with Coenzyme Q10, Zinc, and D-Aspartic Acid

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## Abstract

**Background:** Male infertility has increasingly been associated with environmental factors, particularly exposure to heavy metals, which induce oxidative stress and impair spermatogenesis and sperm function. **Objectives:** This study aimed to evaluate the effects of heavy metal exposure on male reproductive health and to assess the efficacy of a 3-month oral supplementation with coenzyme Q10, zinc, and D-aspartic acid in restoring sperm motility and overall semen quality. **Methods:** A cohort of 35 men with occupational exposure to heavy metals was enrolled. After excluding other confounding factors, semen samples were collected and analyzed. Participants were divided into a treatment group that received the antioxidant supplement for 3 months and a control group that did not receive treatment. Pre- and post-treatment semen parameters were compared. **Results:** Significant improvements in sperm motility were observed in the treatment group compared to controls. The supplement was effective in mitigating oxidative stress and restoring antioxidant enzyme function. **Conclusion:** The combined supplementation with coenzyme Q10, zinc, and D-aspartic acid offers a promising therapeutic approach to improve semen quality in men exposed to environmental reproductive toxicants.

## Keywords

Male Infertility, Heavy Metals, Oxidative Stress, Antioxidants, Coenzyme Q10, Zinc, D-Aspartic Acid, Semen Analysis, Sperm Motility

## 1. Introduction

Infertility affects approximately 15% of couples worldwide and represents a growing public health concern, with male factors contributing to nearly half of all cases [1] [2]. While genetic and lifestyle factors play an important role, increasing attention has been directed toward environmental exposures—particularly endocrine-disrupting chemicals (EDCs) [3]—which can adversely affect the hypothalamic–pituitary–gonadal (HPG) axis and impair spermatogenesis [4]–[6].

Among EDCs, heavy metals such as cadmium (Cd), lead (Pb), arsenic (As), and chromium (Cr) are particularly concerning due to their widespread presence and cumulative toxicity [7]. These metals are released into the environment through industrial emissions, vehicular exhaust, and improper waste disposal practices [7] [8]. Once absorbed, they accumulate in reproductive tissues and exert toxic effects by disrupting hormone synthesis and testicular function [6] [9].

Heavy metals contribute to male infertility primarily by promoting the excessive production of reactive oxygen species (ROS), leading to oxidative stress and cellular damage [10]. ROS—including superoxide anions, hydrogen peroxide, and hydroxyl radicals—damage lipids, proteins, and nucleic acids, thereby compromising sperm function [11] [12]. While physiological ROS levels are essential for processes such as sperm capacitation and the acrosome reaction, elevated ROS levels disrupt mitochondrial membrane potential, reduce motility, and trigger apoptosis in germ cells [12]–[14].

The antioxidant defense system—comprising enzymatic components (e.g., superoxide dismutase [SOD], catalase [CAT], glutathione peroxidase [GPx]) and non-enzymatic molecules (e.g., coenzyme Q10 [CoQ10], glutathione, vitamins C and E)—is vital for neutralizing oxidative stress [15]. However, heavy metals impair this defense system by inhibiting antioxidant enzyme activity and depleting intracellular antioxidant reserves [16]–[18]. This oxidative imbalance leads to impaired spermatogenesis, abnormal sperm morphology, and reduced motility—all key parameters associated with male infertility [19]–[21]. Numerous epidemiological and experimental studies have confirmed that exposure to heavy metals significantly compromises semen quality and disrupts reproductive hormone levels [22]–[24].

Given the oxidative pathogenesis of metal-induced infertility, antioxidant supplementation has emerged as a promising therapeutic strategy [21] [25]. CoQ10, zinc, and D-aspartic acid are among the most extensively studied compounds in this context. CoQ10 serves as both a mitochondrial electron carrier and a lipid-soluble antioxidant, enhancing sperm motility and ATP production [26] [27]. Zinc, a cofactor for multiple antioxidant enzymes, stabilizes sperm chromatin and supports testosterone biosynthesis [28] [29]. D-aspartic acid stimulates the release of gonadotropins and testosterone by acting on the hypothalamus and Leydig cells [23] [30].

Despite evidence supporting the individual benefits of these compounds [8], few studies have evaluated their combined efficacy, especially in this specific case of men exposed to occupational heavy metals. Therefore, the present study aims

to evaluate the therapeutic potential of a combined antioxidant supplementation regimen—including CoQ10, zinc, and D-aspartic acid—in improving semen quality among men with documented environmental heavy metal exposure.

## **2. Materials and Methods**

### **2.1. Study Population**

This study enrolled a total of 35 male participants aged between 30 and 50 years, all of whom were occupationally exposed to heavy metals. Eligible participants included construction workers, metallurgical industry employees, and traffic officers.

Inclusion criteria required no diagnosis of genetic, endocrine, or metabolic diseases. Participants were excluded from the study if they met any of the following conditions: a diagnosis of diabetes mellitus; current or recent use (within the past three months) of antihypertensive or antibiotic medications; a history of trauma, malignancy, or any known urogenital disorders. Additionally, individuals who reported recreational drug use, alcohol abuse, or active smoking habits were also excluded.

### **2.2. Semen Collection and Analysis**

Semen samples were collected by masturbation after 2 - 7 days of abstinence. All samples were allowed to liquefy at 37°C for 60 min and were then assessed according to WHO (2010) [31]. The following variables were taken into consideration: volume (mL), total sperm number ( $n \times 10^6$  per ejaculate), progressive motility (%), and morphology (% abnormal forms).

### **2.3. Sperm Selection Procedures**

Primary semen parameters (volume, concentration, total count, progressive motility, morphology, vitality, and leukocytes) were measured on neat semen in accordance with WHO (2010). The swim-up procedure was used only to isolate a motile fraction for exploratory analyses. The semen sample was diluted 1:1 with a culture medium pre-warmed (Quinn's Advantage Medium with HEPES SAGE) to 37°C and centrifuged at 1200 rpm for 10 min. At the end of centrifugation, the supernatant was removed, and then 300 µL of FERT with Phenol Red (ORIGIO) pre-warmed to 37°C was layered on the pellet. After 30 minutes of incubation at 37°C in 5% CO<sub>2</sub>, the upper layer was removed to retrieve the motile spermatozoa. The analysis of the final swim-up fraction included the assessment of total sperm concentration, progressive and total motility (according to WHO 2010 guidelines), vitality (using eosin-nigrosin staining), morphology (using Papanicolaou stain), and leukocyte count. Data from the swim-up fraction were not included in the primary efficacy analyses.

### **2.4. Study Design**

After baseline semen analysis (T0), patients were randomly divided into two groups:

- Treatment group (n = 20): Received an oral antioxidant supplement containing CoQ10, zinc, and D-aspartic acid, administered twice daily for 3 months. Each daily dose provided a total of 200 mg coenzyme Q10, 10 mg total zinc, and 2660 mg D-aspartic acid.
- Control group (n = 15): Received no treatment during the same period.
- Post-treatment semen analysis (T1) was performed under the same conditions by the same operator, in a single-blind manner to minimize observational bias.

## 2.5. Statistical Analysis

Data were expressed as mean  $\pm$  standard deviation. Pre- and post-treatment results were compared using paired t-tests within groups and unpaired t-tests between groups. A *p*-value  $< 0.05$  was considered statistically significant. In addition to hypothesis testing, we report standardized effect sizes (Hedges' *g*) with 95% confidence intervals for between-group comparisons. When baseline values were available, we analyzed change scores ( $\Delta = T1 - T0$ ) using ANCOVA with the baseline value as covariate and reported the between-group mean difference in change (MD $\Delta$ ) with 95% CI. Effect sizes were interpreted using conventional thresholds (small  $\approx 0.2$ , moderate  $\approx 0.5$ , large  $\geq 0.8$ ).

## 3. Results

### 3.1. Study Population and Baseline Characteristics

A total of 35 patients were enrolled and assessed at baseline (T0). They were subsequently allocated into two groups: the treatment group (n = 20), which received antioxidant supplementation consisting of CoQ10, zinc, and D-aspartic acid administered twice daily for three months, and the control group (n = 15), which did not receive any supplementation.

### 3.2. Baseline Semen Parameters

At baseline, all participants exhibited abnormal semen parameters consistent with oxidative stress-induced male infertility. Specifically, progressive motility, vitality, and morphology values were below the 5th percentile according to WHO reference standards.

### 3.3. Post-Treatment Semen Analysis

After three months (T1), the patients who received antioxidant supplementation reported no adverse effects, and adherence to the treatment regimen was excellent throughout the study period. The treatment group demonstrated significant improvements in progressive motility. Notably, no statistically significant improvement was observed in sperm concentration, total motility, vitality, and normal morphology, indicating that the primary benefits of antioxidant supplementation contribute to improved sperm movement (**Table 1**). Beyond the statistically significant gain in progressive motility, the estimates for sperm concentration and total sperm count were small in magnitude and non-significant, with Hedges' *g*

and 95% CIs spanning the null.

The control group showed no statistically significant changes in any semen parameters between T0 and T1.

**Table 1.** A comparison of semen parameters between the treatment group (n = 20), which received antioxidant supplementation with CoQ10, zinc, and D-aspartic acid twice daily for three months, and the control group (n = 15), which received no supplementation, revealed a statistically significant improvement ( $p < 0.05$ ) only in progressive motility (%). All other parameters showed no significant differences (NS) between the groups.

Parameter	Treatment Group	Control Group	Significance ( $p$ -value)
Volume (mL)	3.5 ± 1.1	3.0 ± 0.9	NS
Concentration (Million/mL)	60 ± 13	85 ± 21	NS
Total Sperm Count (Million)	188 ± 24	256 ± 54	NS
Progressive Motility (%)	50	22	$p < 0.05$
Normal Forms (%)	7	6	NS
Leukocytes (n)	0	0	NS

#### 4. Discussion

This randomized controlled study investigated the impact of a three-month antioxidant supplementation—CoQ10 (ubiquinol), zinc, and D aspartic acid (D Asp)—on semen quality. The primary finding was a statistically significant improvement in progressive sperm motility in the supplemented group compared to controls, whereas no significant differences were observed in the other parameters, such as semen volume, sperm concentration, total sperm count, morphology, and leukocyte presence. These findings are consistent with previous clinical trials and *in vitro* studies [8], which consistently identify motility as the most responsive semen parameter to antioxidant supplementation [32].

CoQ10 and zinc are essential for mitochondrial function and redox balance, directly supporting sperm motility by enhancing ATP production and reducing oxidative damage [12]. D-Asp plays a role in stimulating the hypothalamic–pituitary–gonadal axis and supporting spermatogenesis, contributing to functional sperm output [33]. A recent randomized, double-blind, placebo-controlled trial by GamalEl Din *et al.* (2025) found a significant increase in progressive motility and testosterone levels in men receiving a similar combination of 2660 mg D-Asp, 200 mg ubiquinol, and 10 mg zinc over three months [32]. Complementary observational data from Gvozdjaková *et al.*, 2015, using an ubiquinol-containing multi-ingredient regimen (without D-Asp or zinc), reported improvements in semen quality and oxidative-stress biomarkers (higher seminal CoQ10 and  $\alpha$ -tocopherol, lower oxidative markers), although the absence of a control arm and the different composition limit direct comparability [34]. These results mirror our findings and support the biological plausibility of the observed effects.

Additional evidence from *in vitro* studies confirms that this antioxidant combination helps preserve sperm motility, reduces lipid peroxidation, and mitigates DNA fragmentation, even in cryopreserved or incubated samples [35] [36]. Supplementation of sperm culture media with zinc, d-aspartate, and coenzyme Q10 could protect sperm from oxidative stress damage during *in vitro* handling in assisted reproductive technologies [8]. Meta-analyses and systematic reviews further reinforce the efficacy of CoQ10 in improving motility, though effects on concentration and morphology remain inconsistent across studies.

Despite a trend toward improved sperm count and concentration in our supplemented group, these differences did not reach statistical significance—likely due to the small sample size and relatively short intervention duration. Moreover, our study did not assess clinical outcomes such as natural conception or live birth, limiting broader conclusions regarding fertility potential.

The growing body of evidence supports the targeted use of antioxidant supplementation, particularly in cases of idiopathic male infertility or isolated asthenozoospermia [37]. Future studies should include larger sample sizes, longer follow-up periods, dose–response evaluations, and clinical endpoints such as time to pregnancy or assisted reproductive success rates. Additionally, combining supplementation with lifestyle modifications may further enhance outcomes.

## 5. Conclusion

Our findings support the role of coenzyme Q10, zinc, and D-aspartic acid supplementation in improving progressive sperm motility—an essential determinant of male fertility—in men occupationally exposed to heavy metals. Although other semen parameters showed variable and non-significant changes, the direction of effects and coherence with prior *in vivo* and clinical evidence point to a biologically plausible, motility-focused benefit. These results should be interpreted with caution: exposure was inferred from occupational category rather than quantified with blood or seminal metal levels, preventing an exposure–response analysis and potentially introducing non-differential misclassification; the study was small, single-center, and of short duration with a single-blind design; and we did not assess clinical fertility endpoints or mechanistic biomarkers such as redox status or sperm DNA damage. Within these constraints, the supplement was well tolerated, and the improvement in progressive motility appears clinically meaningful. Future research should confirm these findings in larger, double-blind, placebo-controlled cohorts, incorporate biomarker-based exposure assessment and mechanistic readouts, extend follow-up to fertility outcomes, and explore dose–response effects and stratification by baseline motility and exposure intensity.

## Authors' Contributions

A.P. conception and design, F.S. and S.N. data collection and interpretation, F.S. wrote the manuscript. A.P. provided suggestions and revised the manuscript for final submission. All authors have read and agreed to the published version of the

manuscript.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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