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Short Communication

Coenzyme Q10 as adjuvant therapy could reduce oxidative stress and enhance sperm quality in cryptorchidism animal models

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Abstract

The role of coenzyme Q10 (CoQ10) as an antioxidant in the context of cryptorchidism is increasingly recognized due to its potential protective effects against oxidative stress, a key contributor to testicular dysfunction in this condition. The aim of this study was to evaluate the antioxidant activity of CoQ10 and its impact on sperm parameters as an adjuvant therapy in a cryptorchidism mouse model. A total of 36 male Sprague Dawley mice were divided into six groups: control (negative control), cryptorchidism (positive control), orchidopexy only, and orchidopexy treated with CoQ10 at 5, 10 and 20 mg/kg body weight (BW). After seven days of induction into the cryptorchidism model, the mice underwent orchidopexy, and CoQ10 was administered orally from day 1 to day 7 post-orchidopexy. At the end of the treatment period, all mice were euthanized, and the left testes were collected for immunohistochemical analysis of malondialdehyde (MDA) and superoxide dismutase (SOD), as well as histological examination and sperm parameter assessment. Testicular tissue damage was assessed using the Cosentino grade, while spermatogenesis was evaluated using the Johnsen scoring system. Additionally, sperm parameters were analyzed from the left testis. MDA expression in the cryptorchidism group was significantly lower than in all CoQ10-treated groups (p<0.001). In contrast, SOD expression was significantly higher in the cryptorchidism group compared to the 10 mg/kg BW and 20 mg/kg BW CoQ10 groups (both had p<0.001). Cosentino grade and Johnsen score showed no significant differences between the control group and the group treated with 20 mg/kg BW CoQ10 (p=0.891 and p=0.123, respectively). Furthermore, the 20 mg/kg BW CoQ10 group had significantly greater sperm concentration and motility compared to the cryptorchidism group (p<0.001 for both). These findings demonstrated that CoQ10 had significant antioxidant activity as an adjuvant therapy in a cryptorchidism mouse model. CoQ10 supplementation could reduce oxidative stress markers, enhance antioxidant enzyme expression, and improve sperm parameters, supporting its potential to mitigate testicular damage associated with cryptorchidism.

Keywords: Cryptorchidism, coenzyme Q10, antioxidant, malondialdehyde, superoxide dismutase

Introduction

Congenital cryptorchidism, or undescended testis, is a condition where one or both testes fail to descend into the scrotum at birth. This condition affects approximately 1–3% of full-term male

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infants and is notably more prevalent in preterm infants, reaching up to 30% [1,2]. The incidence naturally declines by about 50% within the first six months of life due to spontaneous testicular descent [3]. However, in cases where descent does not occur, medical intervention is necessary. If left untreated, cryptorchidism increases the risk of infertility and testicular malignancy [4].

Orchidopexy remains the primary treatment for cryptorchidism [4], yet testicular damage can persist due to prolonged inflammatory responses. Reactive oxygen species (ROS)-induced apoptosis contributes to testicular atrophy and dysfunction [5], exacerbated by heat-induced oxidative stress [6]. Antioxidant therapy may counteract ROS-mediated damage, thereby preserving fertility in cryptorchidism [7,8].

Coenzyme Q10 (CoQ10), a well-studied antioxidant, has demonstrated protective effects against oxidative stress in testicular ischemia [9]. Its role in cryptorchidism is gaining interest, as it enhances antioxidant enzyme activity such as superoxide dismutase (SOD) and catalase (CAT), while reducing oxidative stress markers like malondialdehyde (MDA) [10-14]. A clinical study has shown that CoQ10 supplementation improved sperm motility and reduced oxidative stress in men with idiopathic oligoasthenospermia, further suggesting its protective effect on sperm quality [15]. To date, no studies have examined CoQ10 administration in a cryptorchidism mouse model. Therefore, given the increasing recognition of CoQ10's therapeutic potential and its role in improving clinical outcomes, the aim of this study was to assess the antioxidant effects of CoQ10 and its role in mitigating oxidative stress and improving sperm quality in a cryptorchidism mouse model.

Methods

Study design and setting

This in vivo experimental study employed a post-test-only control group design. The research was conducted at the Experimental Animal Research Laboratory, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia, in 2024. The aim of this study was to investigate the effects of different doses of CoQ10 following orchidopexy in a surgically induced cryptorchidism mouse model. The male Sprague Dawley mice were randomly allocated into six groups, each consisting of six animals. Surgical procedures to induce cryptorchidism and subsequent orchidopexy were performed under general anesthesia. CoQ10 supplementation was administered orally for seven days post-surgery, with doses varying according to the experimental groups. The primary outcomes measured included histopathological evaluation of testicular tissue using Cosentino and Johnsen scoring systems, as well as immunohistochemical analysis of MDA and SOD expression. Additionally, sperm concentration and motility were assessed to evaluate the functional impact on spermatogenesis. The study was conducted in accordance with the animal research: reporting of in vivo experiments (ARRIVE) guidelines for animal research.

Animal preparation and sampling

In this experimental study, the number of test animals in each group was determined using Federer's formula. Based on this calculation, six groups were established, with each initially consisting of four mice. However, to account for potential dropout cases, the sample size was adjusted to six mice per group, resulting in a total of 36 mice. A total of 36 male Sprague Dawley mice were obtained from Veteriner Farma in Surabaya, Indonesia, and transported to Malang in an air-conditioned vehicle. Before the experiment began, the animals underwent a one-week acclimatization period in the laboratory. They were housed in cages at 25°C, with six mice per unit, and provided with adequate nutrition.

Eligibility criteria, randomization and study groups

The inclusion criteria consisted of healthy male mice, aged six weeks with a body weight between 130 and 200 grams, and anatomically normal testes on both sides. The exclusion criteria included mice that died or developed infections during the study. Mice were assigned to each group using a simple randomization technique. A total of 36 male Sprague Dawley mice were randomly assigned to six groups: (1) control (negative control); (2) cryptorchidism (positive control); (3) orchidopexy only (orchidopexy A); (4) orchidopexy with CoQ10 at 5 mg/kg body weight (BW)

(orchidopexy B); (5) orchidopexy with CoQ10 at 10 mg/kg BW (orchidopexy C); and (6) orchidopexy with CoQ10 at 20 mg/kg BW (orchidopexy D).

Cryptorchidism and orchidopexy animal model

The cryptorchidism model was surgically induced under general anesthesia and administered intraperitoneally using ketamine HCl at a dose of 75 mg/kg. An ilioinguinal incision was made to displace the testes from the scrotum into the abdominal cavity, where they were secured using 4.0 silk sutures. The abdominal wall was then closed with a two-layer suture technique, employing 4.0 polyglycolic acid and 4.0 polypropylene. After a seven-day period, orchidopexy was performed using the same anesthetic protocol as explained previously [16]. The previously placed sutures were removed, and the testes were repositioned into the scrotum and reattached using 4.0 silk sutures. The abdominal closure was completed again using the same two-layer suture technique to ensure consistency in the surgical procedure [16].

Coenzyme Q10 preparation and intervention

A CoQ10 solution (100 mg/125 mL) (America Medic and Science Co, Woodinville, USA) was used for dose preparation. Mice in the orchidopexy B group received 5 mg/kg BW of CoQ10 daily, while those in the orchidopexy C received 10 mg/kg BW and D group received 20 mg/kg BW per day for seven consecutive days post-surgery. The supplementation was administered via oral gavage for seven consecutive days following orchidopexy.

Data collection and outcome measurements

After seven days following the treatment, the mice were anesthetized with chloroform, and the left testis was collected for histopathological staining to assess the Cosentino and Johnson scoring system, as well as immunohistochemical analysis of MDA and SOD expression. Sperm samples were collected by making an incision in the left testicular epididymis to assess sperm concentration and motility. Subsequently, the animals were euthanized using cervical dislocation.

Immunohistochemistry of MDA and SOD expression

Immunohistochemical analysis was conducted to assess MDA and SOD expression in testicular tissue. Monoclonal anti-MDA and polyclonal anti-SOD antibodies (Abcam, Waltham, MA, USA) were used. Tissue sections were deparaffinized, rehydrated, and subjected to heat-induced epitope retrieval in citrate buffer. After phosphate-buffered saline washes, endogenous peroxidase activity was blocked with 0.3% hydrogen peroxide. Sections were incubated with primary antibodies (1:100) for 90 minutes at room temperature, followed by a biotinylated secondary antibody and avidin-biotin peroxidase complex (LSAB System HRP, Dako, Carpinteria, CA, USA). The complex was visualized using 3,3′-diaminobenzidine (DAB) substrate, which produces a brown precipitate indicating positive expression. Counterstaining was done with hematoxylin, followed by dehydration and mounting. Positively stained cells were quantified at 400× magnification and expressed as the number of cells per high-power field.

Histopathological of testicular tissue damage and spermatogenesis

Following extraction, half of the left testis from each mouse was fixed in a 10% formalin solution to preserve tissue integrity. The samples were then subjected to gradual dehydration using increasing ethanol concentrations before being embedded in paraffin. A blinded pathologist sectioned the embedded tissues into 4 µm-thick slices for further analysis. The sections were stained with hematoxylin and eosin (H&E) and examined under a light microscope. Testicular tissue damage was assessed using the Cosentino scoring system [17], which evaluates structural alterations and classifies histopathological changes into four categories: (1) grade 1 – intact testicular structure with a well-organized arrangement of germinal cells; (2) grade 2 – disrupted organization of germinal cells that appear non-cohesive, along with densely packed seminiferous tubules; (3) grade 3 – sloughing of disorganized germinal cells, reduced nuclear size due to pyknosis, and poorly defined seminiferous tubule borders; and (4) grade 4 – tightly packed seminiferous tubules exhibiting coagulative necrosis of germinal cells [17].

Additionally, spermatogenesis was quantified using the Johnsen scoring system [18,19], a ten-point scale that assesses the cellular composition within the seminiferous tubules. The scoring system ranges from 1 to 10 based on the presence and maturity of germ cells: (1) tubular

sclerosis with no seminiferous epithelial cells; (2) only Sertoli cells; (3) spermatogonia only; (4) arrest at primary spermatocyte stage; (5) presence of spermatocytes without spermatids; (6) arrest at spermatid stage with no late spermatids; (7) numerous early but no late spermatids; (8) few late spermatids; (9) disorganized epithelium with abundant late spermatids; and (10) complete spermatogenesis. Detailed scoring is explained elsewhere [19].

Sperm concentration

A portion of the epididymal sperm suspension was fixed using 10% formalin in phosphate-buffered saline, and 400 µL of the suspension was mixed with formaldehyde (Sigma, Missouri, MO, USA) for stabilization. Then, 10 µL of the diluted sample was loaded into a Neubauer counting chamber using a Pasteur pipette (Thoma Assistant, Sondheim vor der Rhön, Germany). Sperm concentration was assessed under a light microscope and expressed as the number of sperm cells per milliliter of suspension [20,21].

Sperm motility

Sperm motility was assessed by placing a drop of the sperm suspension into a Neubauer chamber. Motility was classified using a four-tiered system based on movement characteristics: rapid progressive motility, slow progressive motility, non-progressive motion, and immobility [21]. For each sample, motility was evaluated across five microscopic fields, and the final score was calculated as the mean of these observations.

Statistical analysis

Normally distributed data were analyzed using one-way analysis of variance (ANOVA), followed by the least significant difference (LSD) post hoc test for intergroup comparisons. Non-normally distributed data were analyzed using the Kruskal-Wallis test, followed by Dunn's post hoc test for pairwise comparisons. All statistical analysis was conducted using SPSS software version 23.0 (IBM, Armonk, NY, USA), with statistical significance set at $p<0.05$.

Results

Effect of coenzyme Q10 on MDA and SOD expression

Significant differences in MDA expression were observed across all groups ($p<0.001$). Expression in the control group was significantly higher than in both the cryptorchidism group ($p<0.001$) and the orchidopexy A group ($p=0.002$) (**Figure 1A**). No significant differences were found between the control group and the orchidopexy B ($p=0.999$) or orchidopexy C ($p=0.983$) groups. In contrast, the orchidopexy D group showed a significant reduction in MDA expression compared to the control group ($p=0.047$). These results indicate that orchidopexy A did not effectively reduce MDA expression, whereas orchidopexy B and C restored levels to those of the control group. Notably, orchidopexy D further suppressed MDA expression below control levels, suggesting that higher doses of CoQ10 may provide additional antioxidant effects. No significant differences were observed between the orchidopexy B and C groups ($p=0.996$) or between the orchidopexy B and D groups ($p=0.073$) (**Figure 1A** and **Figure 2**), indicating that CoQ10 supplementation at doses between 5 and 20 mg/kg BW had comparable effects. Thus, the minimum effective dose for reducing MDA expression was 5 mg/kg BW.

The comparison of SOD expression among all groups revealed significant differences ($p<0.001$). Expression in the control group was significantly lower than that in the cryptorchidism group ($p=0.005$) and significantly higher than in the orchidopexy D group ($p=0.007$) (**Figure 1B**). No significant differences were observed between the control group and the orchidopexy A ($p=0.231$), orchidopexy B ($p=0.316$), or orchidopexy C ($p=0.617$) groups. SOD expression was significantly reduced within the cryptorchidism group compared to the orchidopexy C and D groups ($p<0.001$), but not significantly different from the orchidopexy A ($p=0.551$) or B ($p=0.435$) groups. Similarly, SOD expression in the orchidopexy A group was significantly lower than in the orchidopexy C ($p=0.006$) and D ($p<0.001$) groups but not significantly different from the orchidopexy B group ($p=0.999$). The orchidopexy B group also showed significantly lower SOD expression than the orchidopexy C ($p=0.01$) and D ($p<0.001$) groups, whereas no significant difference was observed between the orchidopexy C and D groups

(p=0.255) (**Figure 1B**). These findings indicate that CoQ10 supplementation at doses of 10 mg/kg and 20 mg/kg effectively enhanced SOD expression, with 10 mg/kg BW identified as the minimum effective dose.

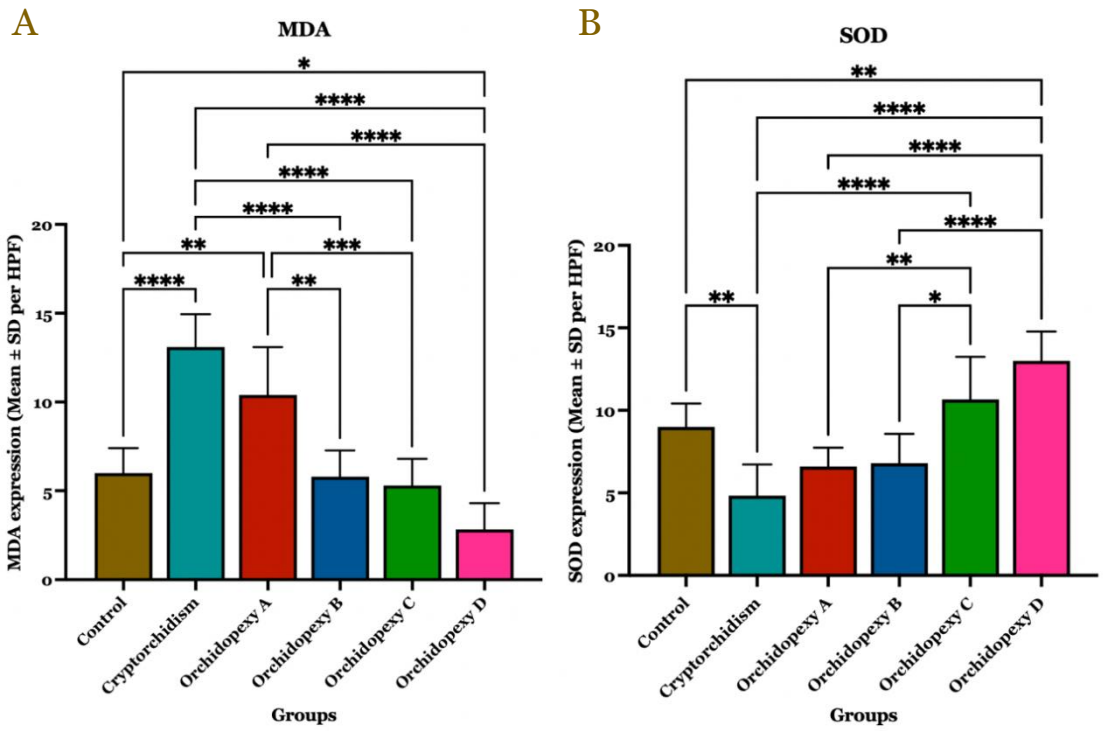

Figure 1. Effect of coenzyme Q10 on the expression of malondialdehyde (MDA) (A) and superoxide dismutase (SOD) (B). Control: healthy negative control; cryptorchidism (cryptorchidism only, as positive control); orchidopexy A: orchidopexy only; orchidopexy B: orchidopexy treated with CoQ10 at 5 mg/kg BW; orchidopexy C: orchidopexy treated with CoQ10 at 10 mg/kg BW; and orchidopexy D: orchidopexy treated with CoQ10 at 20 mg/kg BW. HPF: high power field. Significant at $^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$; $^{****}p<0.0001$.

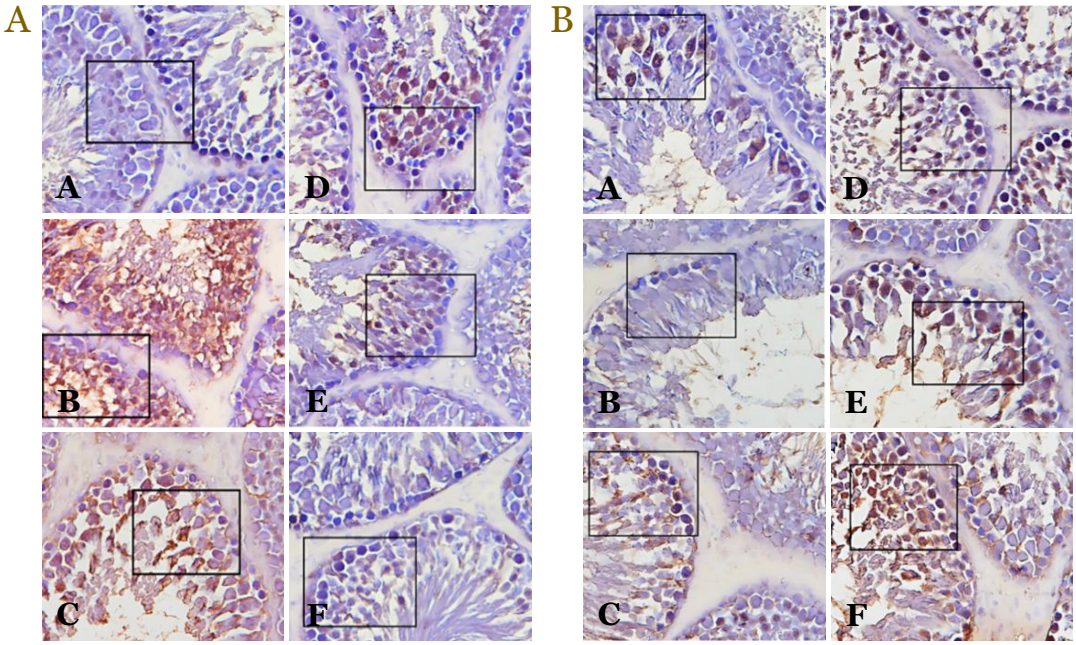

Figure 2. Expression of malondialdehyde (MDA) and superoxide dismutase (SOD) among groups. (A) Immunohistochemical staining of MDA expression in germ cells at 400× magnification. Brown-stained cells indicate positive MDA expression, whereas blue-stained cells represent those that do not express MDA. (B) Immunohistochemical staining of SOD expression in germ cells at 400× magnification. Study groups (A) control: healthy negative control; (B) cryptorchidism (cryptorchidism only, as positive control); (C) orchidopexy A: orchidopexy only; (D) orchidopexy treated with CoQ10 at 5 mg/kg BW; (E) orchidopexy treated with CoQ10 at 10 mg/kg BW; and (F) orchidopexy treated with CoQ10 at 20 mg/kg BW.

Effect of coenzyme Q10 on testicular tissue damage and spermatogenesis

The evaluation of testicular damage using the Cosentino scoring system revealed significant differences among groups (p<0.001), and the comparisons between groups are presented in **Figure 3A**. The Cosentino grade in the control group was significantly higher compared to the orchidopexy A (p<0.001), orchidopexy B (p<0.001), and orchidopexy C (p<0.001) groups. However, no significant differences were found between the control group and the cryptorchidism (p=0.495) or orchidopexy D (p=0.891) groups. The cryptorchidism group showed significantly lower Cosentino grades compared to the orchidopexy A (p<0.001) and orchidopexy C (p<0.001) groups but not compared to the orchidopexy D group (p=0.972). The orchidopexy A group had significantly lower Cosentino grades than the orchidopexy B (p=0.014), orchidopexy C (p=0.034), and orchidopexy D (p<0.001) groups. No significant difference was observed between the orchidopexy B and C groups (p=0.999), while a significant decrease was noted between the orchidopexy C and D groups (p=0.002) (**Figure 3A**). These results suggest that CoQ10 at a dose of 20 mg/kg BW had the most substantial effect in reducing testicular damage, as reflected by the Cosentino score.

The evaluation of spermatogenesis, assessed using the Johnsen scoring system based on the cellular composition of the seminiferous tubules, demonstrated significant differences among groups (p<0.001), and the comparisons between groups are presented in **Figure 3B**. The Johnsen score in the control group was significantly higher than those in the cryptorchidism (p<0.001), orchidopexy A (p<0.001), orchidopexy B (p<0.001), and orchidopexy C (p<0.001) groups, but did not differ significantly from the orchidopexy D group (p=0.123). The cryptorchidism group exhibited a significantly lower score than the orchidopexy A group (p=0.03).

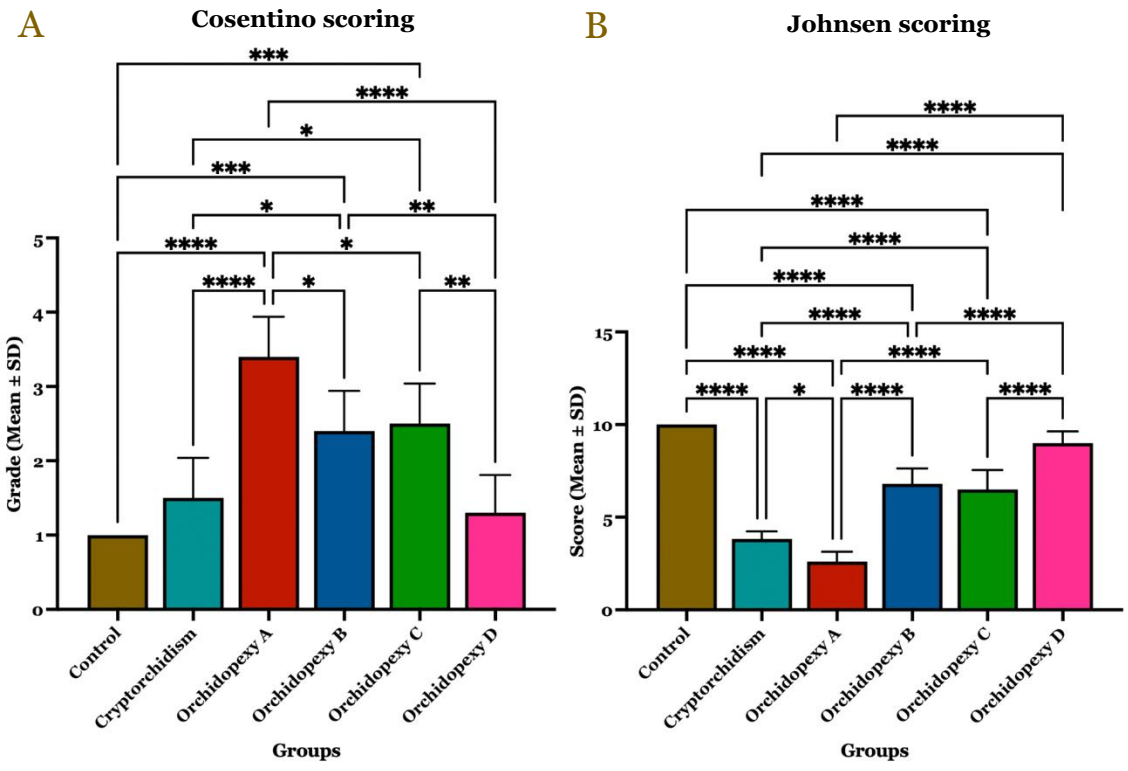

Figure 3. Effect of coenzyme Q10 on testicular tissue damages and spermatogenesis. (A) Testicular tissue damage assessment using the Cosentino scoring system across experimental groups. (B) Spermatogenesis evaluation based on the Johnsen score for each group. Control: healthy negative control; cryptorchidism (cryptorchidism only, as positive control); orchidopexy A: orchidopexy only, untreated; orchidopexy B: orchidopexy treated with CoQ10 at 5 mg/kg BW; orchidopexy C: orchidopexy treated with CoQ10 at 10 mg/kg BW; and orchidopexy D: orchidopexy treated with CoQ10 at 20 mg/kg BW. Significant at $^{*}p$<0.05; $^{**}p$<0.01; $^{***}p$<0.001; $^{****}p$<0.0001.

Meanwhile, the score in the orchidopexy A group was significantly higher compared to the orchidopexy B (p<0.001), orchidopexy C (p<0.001), and orchidopexy D (p<0.001) groups. No significant difference was found between the orchidopexy B and orchidopexy C groups (p=0.967), while a significant increase was observed between the orchidopexy C and orchidopexy D groups (p<0.001) (**Figure 3B**). These findings suggest that CoQ10 supplementation at 5 mg/kg BW and 20 mg/kg BW had a notable effect on spermatogenesis, as reflected by improvements in the Johnsen score (**Figure 4**).

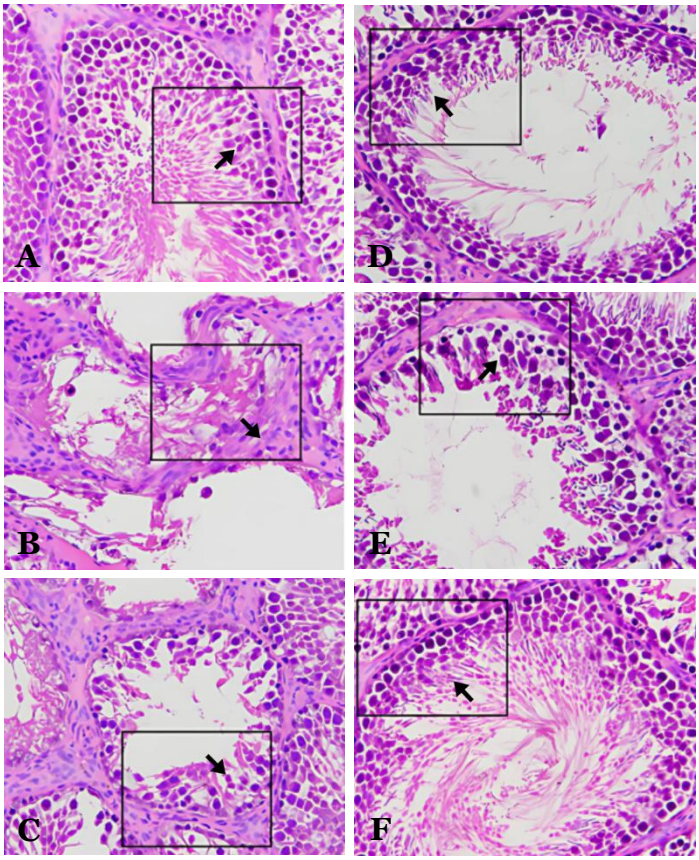

Figure 4. Hematoxylin and eosin (H&E) staining of testicular sections at 400× magnification. Study groups (A) control: healthy negative control; (B) cryptorchidism (cryptorchidism only, as positive control); (C) orchidopexy A: orchidopexy only, untreated; (D) orchidopexy treated with CoQ10 at 5 mg/kg BW; (E) orchidopexy treated with CoQ10 at 10 mg/kg BW; and (F) orchidopexy treated with CoQ10 at 20 mg/kg BW. Black arrows show signs of testicular tissue restoration and active spermatogenesis in most seminiferous tubules.

Effect of coenzyme Q10 on sperm concentration and sperm motility

The assessment of sperm concentration revealed significant variations among groups (p<0.001), as presented in **Figure 5A**. The control group exhibited significantly higher sperm concentration compared to the cryptorchidism (p<0.001), orchidopexy A (p<0.001), orchidopexy B (p<0.001), orchidopexy C (p<0.001), and orchidopexy D (p<0.001) groups. Additionally, sperm concentration in the orchidopexy A group was significantly higher than in the orchidopexy B (p=0.007), orchidopexy C (p=0.001), and orchidopexy D (p<0.001) groups. No significant difference was observed between the orchidopexy B and orchidopexy C groups (p=0.716), whereas a significant increase was noted between the orchidopexy C and orchidopexy D groups (p=0.003) (**Figure 5A**). These findings suggest that CoQ10 supplementation at doses of 5 mg/kg BW and 20 mg/kg BW had a notable impact on sperm concentration.

The assessment of sperm motility also revealed significant differences across groups (p<0.001), as presented in **Figure 5B**. The control group exhibited significantly higher sperm motility compared to the cryptorchidism (p<0.001), orchidopexy A (p<0.001), orchidopexy B (p<0.001), orchidopexy C (p<0.001), and orchidopexy D (p=0.001) groups. Sperm motility in the orchidopexy A group was significantly higher than in the orchidopexy B (p=0.01), orchidopexy C

(p<0.001), and orchidopexy D (p<0.001) groups. A significant difference was also observed between the orchidopexy B and orchidopexy C groups (p<0.001), while no significant difference was found between the orchidopexy C and orchidopexy D groups (p=0.306) (**Figure 5B**). These results indicate that all doses of CoQ10 influenced sperm motility, underscoring its potential to improve sperm parameters following orchidopexy.

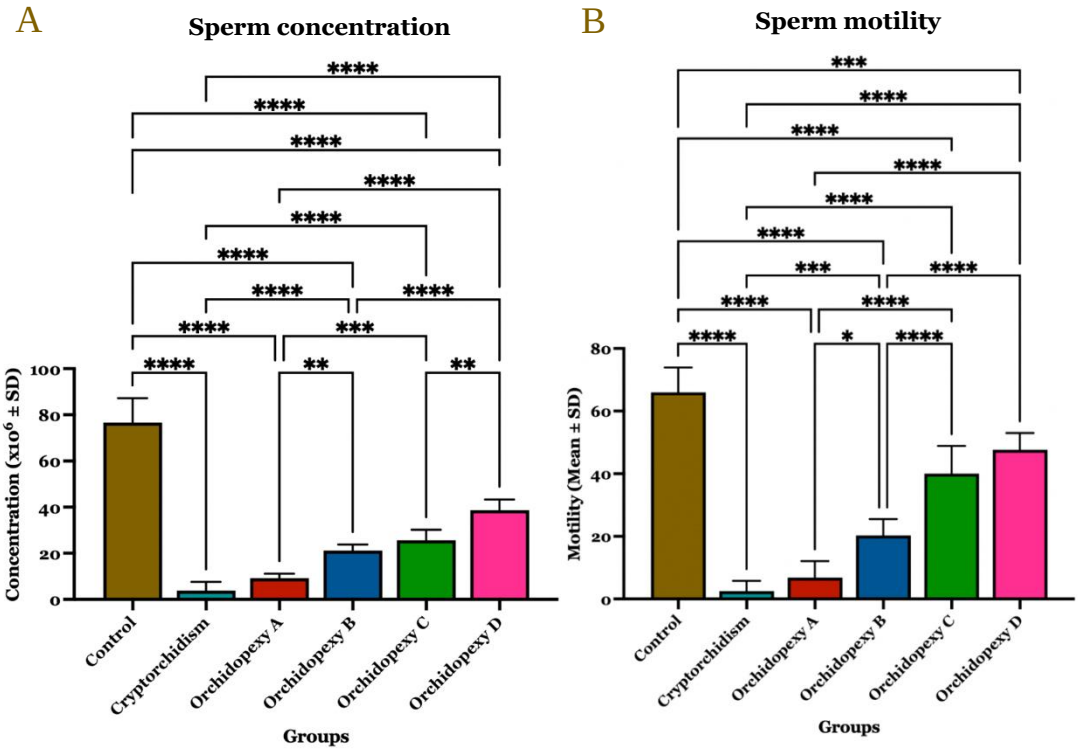

Figure 5. Effect of coenzyme Q10 on sperm concentration and motility. (A) Sperm concentration across groups. (B) Sperm motility across groups. Control: healthy negative control; (2) cryptorchidism (cryptorchidism only, as positive control); orchidopexy A: orchidopexy only, untreated; orchidopexy B: orchidopexy treated with CoQ10 at 5 mg/kg BW; orchidopexy C: orchidopexy treated with CoQ10 at 10 mg/kg BW; and orchidopexy D: orchidopexy treated with CoQ10 at 20 mg/kg BW. Significant at $^{*}p$<0.05; $^{**}p$<0.01; $^{***}p$<0.001; $^{****}p$<0.0001.

Discussion

Several studies have indicated that orchidopexy alone does not eliminate the risk of complications, such as postoperative testicular atrophy [6,22,23]. The ORCHESTRA study, conducted by a study group from Oxford, UK, reported similar findings in cases of cryptorchidism treated with orchidopexy [6]. Among 294 cryptorchidism cases, nine patients developed testicular atrophy despite undergoing the procedure, with atrophy defined as a reduction in testicular size exceeding 50% of the preoperative measurement [6]. Additionally, men with idiopathic oligozoospermia and a history of cryptorchidism have been found to exhibit significantly higher levels of sperm DNA damage [24]. The rise in testicular temperature and heightened reactive oxygen species (ROS) levels in these individuals indicate that oxidative stress within the semen is a key factor contributing to sperm DNA damage [25,26].

MDA is a key end product of lipid peroxidation and serves as a sensitive biomarker for tissue injury, demonstrating a positive correlation with the extent of oxidative tissue damage [16,27]. This study observed significantly higher MDA levels in the testes of cryptorchidism-induced mice compared to the control group. A study has clearly demonstrated that elevated MDA levels in the ipsilateral testis following testicular torsion indicate increased oxidative stress [14]. The results of this study are consistent with a previous study, reinforcing the role of oxidative stress in testicular damage [11]. To counteract this, CoQ10 was administered as an antioxidant, leading to a dose-dependent reduction in MDA levels across doses ranging from 5 mg to 20 mg. This aligns with earlier findings demonstrating that antioxidant treatment, followed by reperfusion,

significantly lowers testicular MDA levels, highlighting the protective effects of CoQ10 against oxidative damage [14].

SOD is an essential antioxidant enzyme that plays a key role in defending cells from oxidative damage by transforming reactive superoxide anion radicals into hydrogen peroxide. This byproduct is subsequently broken down into water and oxygen by catalase, thereby minimizing cellular oxidative stress [13,28]. In this study, SOD expression in the control group was significantly reduced in the cryptorchidism group and markedly elevated in the orchidopexy D group. Additionally, the orchidopexy B group exhibited significantly lower SOD expression compared to the orchidopexy C and orchidopexy D groups, while no significant difference was observed between the orchidopexy C and orchidopexy D groups. These findings indicate that orchidopexy alone does not significantly impact SOD expression, whereas the administration of CoQ10 effectively enhances SOD levels, acting as a scavenger for oxygen-derived free radicals.

Testicular tissue damage and the spermatogenesis process were evaluated using the Cosentino and Johnsen scoring systems, respectively. In this study, based on Cosentino grading, the most severe testicular tissue damage was observed in the orchidopexy-only group rather than in the cryptorchidism group. This finding suggests that testicular damage can continue to progress even after orchidopexy. The association between testicular inflammation and oxidative damage is likely due to the production of ROS in ischemia-reperfusion-like conditions experienced during orchidopexy [29]. Histological analysis revealed testicular tissue repair following CoQ10 administration, and at a dose of 20 mg/kg BW, no significant differences were observed in Cosentino scores. This suggests that CoQ10 played a role in facilitating testicular tissue recovery. These findings are consistent with a previous study [30], which investigated the effects of CoQ10 in a heat-stress model and found that CoQ10 not only ameliorated oxidative stress and inflammatory responses but also significantly improved histopathological outcomes in rat testicular tissues. Furthermore, the Johnsen score analysis indicated that orchidopexy alone was insufficient to fully restore spermatogenesis. However, CoQ10 administration at a dose of 20 mg/kg BW significantly enhanced the spermatogenesis process, showing no significant difference compared to the normal control group.

This study observed an increase in sperm concentration and motility in the orchidopexy B, orchidopexy C, and orchidopexy D groups. The administration of CoQ10 at doses starting from 5 mg/kg BW significantly improved sperm concentration and motility compared to the orchidopexy-only groups. These findings align with previous studies demonstrating the protective effects of CoQ10 against reproductive toxicity induced by various agents. For example, a study [29] reported that exogenous CoQ10 administration ameliorated testicular damage and protected against oxidative stress caused by lead acetate exposure [22]. Similarly, an earlier study highlighted CoQ10's role in preventing oxidative damage to the sperm plasma membrane, thereby enhancing sperm motility and viability [31]. Since sperm cells rely heavily on mitochondrial respiration for ATP production, interventions that support mitochondrial health, such as CoQ10 supplementation, are essential. Another study [31] demonstrated that CoQ10 supplementation positively influenced mitochondrial function, leading to improved sperm motility and reduced DNA fragmentation [32]. Additionally, CoQ10 has been shown to support sperm health by enhancing cellular energy supply while mitigating apoptosis in male germ cells [15]. However, the findings of this study indicate that CoQ10 administration for seven days was not sufficient to fully restore sperm concentration and motility to levels comparable to the control group.

CoQ10 is a naturally occurring antioxidant and a vital component of the electron transport chain. It has been shown to exert protective effects on the testes against various harmful conditions, including sodium arsenite toxicity, ischemia/reperfusion injury, and exposure to magnetic fields [22]. A study [12] reported that CoQ10's antiapoptotic properties stem from its ability to enhance ATP production while preventing mitochondrial depolarization and DNA fragmentation [12]. Furthermore, CoQ10 prevents cell death by inhibiting the nuclear translocation of pro-apoptotic proteins and suppressing mitochondrial complex I activity. Another study [11] further demonstrated that CoQ10 mitigates oxidative stress in the testes by enhancing antioxidant enzyme activity and preventing lipid peroxidation [11]. This protective mechanism helps preserve Leydig cell function, thereby maintaining testosterone secretion [33].

The decrease in MDA levels following CoQ10 supplementation is likely attributed to its ability to enhance the antioxidant defense system, particularly through the upregulation of SOD expression, which plays a crucial role in mitigating free radical toxicity. The primary mechanism of CoQ10 may involve scavenging free radicals, inhibiting their formation, and exerting protective effects against apoptosis in various tissues and cells [34]. CoQ10 has emerged as a promising adjuvant treatment following orchidopexy due to its potent antioxidant properties [35]. Therefore, incorporating CoQ10 as an adjunct therapy may help optimize testicular function and improve long-term reproductive outcomes in patients undergoing orchidopexy.

However, this study has certain limitations. First, we did not assess MDA and SOD expression in the contralateral testes, which limits our understanding of CoQ10's antioxidant activity in the non-cryptorchid testis. Second, this study remains an experimental preclinical investigation, serving as a preliminary step toward potential clinical trials. While the promising in vivo findings, both at the cellular and laboratory levels, suggest therapeutic potential, further research is necessary to establish its clinical applicability. Moreover, further studies should focus on elucidating the underlying signaling pathways involved in CoQ10-mediated oxidative stress reduction to enhance its potential clinical applications.

Conclusion

This study demonstrated that CoQ10 exhibits significant antioxidant activity as an adjuvant therapy in a cryptorchidism mouse model. CoQ10 supplementation effectively reduced oxidative stress markers, enhanced antioxidant enzyme expression, and improved sperm parameters, suggesting its potential role in mitigating testicular damage associated with cryptorchidism. These findings support the therapeutic potential of CoQ10 in preserving testicular function, highlighting its promise as a complementary treatment following orchidopexy. However, further research is needed to determine its clinical applicability and establish optimal dosing strategies.

Ethics approval

This study was approved by the Ethical Committee of Universitas Brawijaya, Malang, Indonesia (No. 052/KEP/UB/2024).

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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