Original Article

The Effect of Coenzyme Q10 on Serum Glutathione Peroxidase Levels and Severity of Acne Vulgaris

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Abstract

Objective: The objective of the study was to study the effect of coenzyme Q10 (CoQ10) supplementation on serum glutathione peroxidase (GSH-Px) levels and the severity of acne vulgaris (AV). **Methods:** A double-blind randomized controlled trial was carried out on 36 patients with AV classified according to severity. These patients were randomly divided into two groups (treatment group = 18 patients treated with tretinoin 0.025% cream and once-daily supplementation with a CoQ10 100 mg tablet; placebo group = 18 patients treated with tretinoin 0.025% cream and a once-daily placebo tablet). Blood samples were taken from a vein and examined by enzyme-linked immunosorbent assay. The study period was 8 weeks. Response to treatment was determined based on serum GSH-Px level and AV severity. The study used a pre- and post-test design for the two groups. The data were processed with SPSS for Windows version 25. **Results:** Administration of CoQ10 to AV significantly improved the severity of AV after 8 weeks compared to a placebo ($P = 0.008$). Serum GSH-Px levels after treatment with CoQ10 increase higher in the study than control group, but the statistical test result showed not significant in the study group ($P = 0.3$) and also control group ($P = 0.07$). **Conclusion:** CoQ10 supplementation may increase serum GSH-Px levels and improve the severity of AV, but there was no relationship between serum GSH-Px levels and the severity of AV.

Keywords: Acne vulgaris, coenzyme Q10, glutathione peroxidase, oxidative stress, tretinoin

Introduction

Acne vulgaris (AV) is a chronic inflammatory disease of the pilosebaceous follicular unit with multifactorial causes.[1] Recent research has shown an increase in total cases among a sample of 26–44-year-old females.[2,3] In Indonesia, in 2008, AV affected 15.3% of cases at the Dermatovenerology clinic of Dr. Kariadi General Hospital, Semarang, representing the tenth most prevalent skin condition.[4]

AV is characterized by inflammatory papules, pustules, and nodules, as well as noninflammatory open or closed comedones. Affected sites are chiefly on the face but can also include the upper arms, trunk, and back.[5] The Indonesian Acne Expert Meeting in 2012 recommended the use of the Lehmann grading system, which categorizes acne as mild, moderate, or severe.[6]

In terms of etiology, four crucial factors are thought to be involved in acne pathology: *Propionibacterium acnes*, responsible for the production of pro-inflammatory mediators by the immune system; sebaceous gland hypersecretion of sebum; hyperkeratosis leading to obstruction of the follicle; and inflammatory factors produced by the skin and immune system. Recent studies have suggested that various mechanisms and molecular pathways link oxidative stress to the pathogenesis of AV: toll-like receptors, peroxisome proliferator-activated receptors, the innate immune system, and mechanistic target of rapamycin.[4] An imbalance in the production of oxygen-derived prooxidants, also known as reactive oxygen species (ROS), and the cellular capacity of antioxidant defense is believed to lead to oxidative stress. Normally, ROS are removed by antioxidant enzymes in the cell, such as glutathione peroxidase (GSH-Px), catalase (CAT), and superoxide dismutase (SOD).[7]

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GSH-Px is a group of important antioxidant enzymes. GSH-Px is the general name of an enzyme family with peroxidase activity, whose main biological role is protection from oxidative damage caused by ROS. The biological functions of GSH-Px are to reduce lipid hydroperoxide to its corresponding alcohol and reduce free hydrogen peroxide to water.[8,9]

Many therapeutic options are available for AV, including topical, systemic, and adjuvant therapies. The Global Alliance to Improve Outcomes in Acne published recommendations for the management of acne as a supplement to the *Journal of the American Academy of Dermatology* in 2003. The update also included a new way of considering acne as a chronic disease, a discussion of the changing role of antibiotics in acne management as a result of concerns about microbial resistance, and factors that affect adherence to acne treatments.[10] Oxidative stress may be implicated in the origin of acne, and antioxidant supplements may be valuable adjuvants in acne treatment.[11]

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a lipid-soluble substance whose primary role is as an essential intermediate of the electron transport system in the mitochondria. Adequate amounts of CoQ10 are necessary for cellular respiration and ATP production. It significantly enhances antioxidant enzymes and regenerates tocopherol and ascorbic acid.[12] A typical CoQ10 dosage is 30–90 mg/day, but the recommended amount can be as high as 200 mg/day, and dosage >150 mg/day provides rapid and sustainable antioxidant and clinical improvement after 8 weeks of supplementation.[13,14]

CoQ10 treatment does not cause serious adverse effects in humans, and new formulations have been developed that increase CoQ10 absorption and tissue distribution. CoQ10 administered by oral and topical.[15] Topical CoQ10 application showed beneficial effects on mitochondrial membrane potential by reaching the vital layers of the skin, exerts antioxidant effects, and maintain the cellular energy levels.[16]

Oral administration of CoQ10 is a frequent antioxidant strategy in many diseases, which may provide a significant symptomatic benefit.[14,15] Therefore, this study investigated the effect of CoQ10 supplementation on serum GSH-Px levels and the severity of AV.

Methods

Research design

This study was performed between December 2019 and February 2020. Thirty-six women clinically diagnosed with AV, who attended the Outpatient Department of Dermatology and Venereology at Dr. Kariadi General Hospital, were enrolled in the study. Before initiation, each participant was informed about the aim of the study and signed an informed consent. Ethical approval for this study was obtained from Dr. Kariadi General Hospital Ethical Committee (380/EC/KEPK-RSDK/2019).

The inclusion criteria were mild-to-moderate-severe AV patients, female, aged 20–40 years, normal body mass index, mild-to-normal stress level (assessed by Beck's Depression Inventory), not taking drugs (antibiotics, anti-inflammatories, beta-blocker antihypertensives, statin antihyperlipidemics, warfarin, vitamins, or antioxidants) in the past 1 month, not pregnant and breastfeeding, not smoking, and willing to take part in the study to completion. The exclusion criteria were patients whose blood samples could not be collected due to technical factors and patients who refused blood sample collection.

The 36 patients were randomly allocated into two groups.

$$N1 = N2 = \left[\frac{(1.96 + 0.84) \times 3.3}{(26.9 - 23.6)}\right]^2$$

$$= 16$$

The minimum sample required was calculated as 16. Anticipating a nonresponse or dropout rate of 10%, a sample size of 18 for each group was set.

The first group of 18 patients was treated with tretinoin 0.025% cream and one CoQ10 100 mg oral tablet per day. The second group of 18 patients was treated with tretinoin 0.025% cream and one oral placebo tablet per day. The use of sunscreen cream with SPF 30 was suggested during the study period.

The diagnosis of AV was based on the total lesion count of comedones, papules, pustules, nodules, and cysts, according to the Lehmann criteria of AV severity. The duration required for each patient to complete the course of treatment was 8 weeks, with clinical and laboratory assessments carried out at baseline and the end of this period. Adverse effects were investigated by asking patients about any abnormal effect that appeared throughout the whole course of treatment.

Sample analysis

Blood samples for GSH-Px analysis were collected between December 2019 and February 2020. Samples of 3 mL were collected by venipuncture and allowed to clot for 2 h overnight at 2°C–8°C before centrifuging for 15 min at 1000 xg and 2°C–8°C. Serum GSH-Px was examined by enzyme-linked immunosorbent assay.

Statistical analysis

The data obtained were processed with SPSS software for Windows version 25 (IBM, New York, USA). Analysis used the paired *t*-test, Wilcoxon test, Mann–Whitney test, McNemar test, and Chi-square test to compare pre- and post-treatment values between the two groups. The significance level was set at $P \leq 0.05$. The Spearman correlation test was used to compare between serum GSH-Px level and severity of AV. The degree of relationship was expressed by the magnitude of the correlation coefficient. Intention to treat analysis was used in this study.

Results

Table 1 shows the demographic characteristics of each group. The mean age in the study group was 25.9 ± 4.52 years, and in the control group 26.5 ± 5.82 years. Statistical test results showed no significant difference in group ages (P = 0.9; Mann–Whitney test). The most common occupation in the study group was student (44.4%) and office worker in the control group (33.3%); statistical results were not significant (P = 0.1; Fisher's exact test). In the study group, 55.6% reported no sun exposure compared to 50% of the control group; the difference was not significant (P = 0.7; χ^2 test).

Figure 1 shows that, in study groups, serum GSH-Px levels higher than in the control group after treatment. Table 2 shows that serum GSH-Px levels increased from 518.3 ± 160.04 pg/mL to 1382.6 ± 740.55 pg/mL in the study group, which was not significant (P = 0.3; Mann–Whitney test). In the control group, levels increased from 549.3 ± 325.16 pg/mL to 1,036.2 ± 646.60 pg/mL, which was also not significant (P = 0.07; Mann–Whitney test). The result showed that the levels of serum GSH-Px in the study group was higher than in control group. But the statistical test results showed not significant.

The serum GSH-Px delta in the study group of 864.3 ± 631.95 pg/mL was significantly higher than the control group delta of 486.9 ± 549.81 pg/mL (P = 0.03; Mann–Whitney test).

Table 3 shows the severity of AV based on the Lehmann scoring criteria in the study and control groups. Statistical test results showed the change in the severity in the study group was significant (P = 0.008; McNemar test), whereas the change in the severity in the control group was not significant (P = 0.05; McNemar test).

Table 3 also shows the average serum GSH-Px level before treatment. The lowest level was in the severe group at 485.4 ± 237.62 pg/mL, whereas the highest level was in the moderate group at 603.4 ± 309.69 pg/mL. Statistical test results showed the differences in serum GSH-Px levels based on the

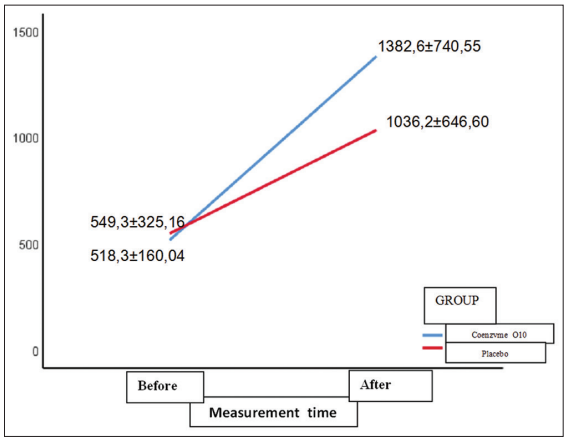

Figure 1: Shows that the control and study groups showed a increase in serum GSH-Px levels from before to after treatment. The Effect Of Coenzyme Q10 on Serum Gluthation Peroxidase Levels and Severity Of Acne Vulgaris

Table 1: Demographic characteristics of the study participants

Characteristic	Group		*P*
	Study (*n*=18)	Control (*n*=18)	
Age (years): mean±SD	25.9±4.52	26.5±5.82	0.9*
median (minimum-maximum)	25 (21-33)	25 (20-40)	
Occupation, *n* (%)			
Doctor	7 (38.9)	4 (22.2)	0.1§
Student	8 (44.4)	5 (27.8)	
Business	1 (5.6)	6 (33.3)	
Midwife	2 (11.1)	1 (5.6)	
Housewife	0 (0.0)	2 (11.1)	
Sun exposure, *n* (%)			
No	10 (55.6)	9 (50.0)	0.7¶
Yes	8 (44.4)	9 (50.0)	

*Mann–Whitney test, §Fisher's exact test, ¶ χ^2 test. SD: Standard deviation

Table 2: Effect of coenzyme Q10 on serum glutathione peroxidase levels

Measurement time	GSH-Px serum level (pg/mL) Mean±SD Median (minimum-maximum)		*P*¥
	Study group (*n*=18)	Control group (*n*=18)	
Before	518.3±160.04	549.3±325.16	0.3
	502.0 (279.7-866.1)	405.6 (286.1-1,221.7)	
After	1,382.6±740.55	1,036.2±646.60	0.07
	1,251.1 (475.7-2,870.0)	778.2 (536.6-2,696.4)	
Delta	864.3±631.95	486.9±549.81	0.03
	754.4 (136.7-2,113.3)	300.6 (131.2-2,275.5)	
P§ before versus after	<0.001	<0.001	

¥Mann–Whitney test, §Wilcoxon test. Delta: GSH-Px serum after – GSH-Px serum before, GSH-Px: Glutathione peroxidase, SD: Standard deviation

Table 3: Average serum glutathione peroxidase level before and after treatment by acne vulgaris severity based on Lehmann scoring criteria

Acne severity	GSH-Px serum level pg/mL Mean±SD; median (minimum-maximum)
Before treatment	
Mild (*n*=12)	512.6±207.54; 434.2 (318.0-1,009.6)
Moderate (*n*=12)	603.4±309.69; 499.7 (301.6-1,221.7)
Severe (*n*=12)	485.4±237.62; 440.6 (279.7-1,189.1)
After treatment	
Mild (*n*=24)	1,249.9±741.28; 944.4 (475.7-2,870.0)
Moderate (*n*=11)	1,152.3±684.06; 936.5 (576.9-?.4)
Severe (*n*=1)	866.1±0.00; 866.1 (866.1-866.1)

Kruskal–Wallis test: Before treatment P=0.7, After treatment P=0.9. GSH-Px: Glutathione peroxidase, SD: Standard deviation

severity of AV before treatment were not significant ($P = 0.7$; Kruskal–Wallis test). After treatment, the highest serum GSH-Px level was in the mild group at 1249.9 ± 741.28 pg/mL. The lowest was in the severe group at 866.1 ± 0.00 pg/mL. Statistical test results showed that the differences in serum GSH-Px levels based on the severity of AV after treatment were also not significant ($P = 0.3$; Kruskal–Wallis test).

Table 4 shows that the lowest GSH-Px delta decrease was 131.17 pg/mL in the control group with severe AV before treatment and moderate AV after treatment. The biggest increase was 2275.53 pg/mL in the control group with moderate AV before and after treatment. Statistical test results showed no correlation between serum GSH-Px level and AV severity ($P = 0.7$).

Table 4: Delta serum glutathione peroxidase and acne severity

Acne severity		Group	Delta serum GSH-Px (pg/mL)
Before	After		
Mild	Mild	Study	406.75
Mild	Mild	Study	423.37
Mild	Mild	Study	2,023.18
Mild	Mild	Study	1,687.71
Mild	Mild	Study	771.23
Mild	Mild	Study	149.69
Mild	Mild	Control	156.30
Mild	Mild	Control	806.32
Mild	Mild	Control	321.17
Mild	Mild	Control	240.32
Mild	Mild	Control	197.99
Mild	Mild	Study	310.45
Moderate	Mild	Study	303.42
Moderate	Moderate	Study	1,040.49
Moderate	Mild	Study	1,560.28
Moderate	Mild	Study	393.91
Moderate	Moderate	Study	156.13
Moderate	Mild	Study	2,113.27
Moderate	Mild	Control	134.3
Moderate	Mild	Control	205.22
Moderate	Mild	Control	1,478.2
Moderate	Moderate	Control	258.62
Moderate	Moderate	Control	328.1
Moderate	Moderate	Control	2,275.53
Severe	Mild	Study	567.31
Severe	Moderate	Study	1,132.96
Severe	Mild	Study	956.2
Severe	Moderate	Study	737.51
Severe	Mild	Study	998.09
Severe	Mild	Study	136.69
Severe	Moderate	Control	199.2
Severe	Moderate	Control	290.83
Severe	Mild	Control	480.83
Severe	Moderate	Control	557.98
Severe	Moderate	Control	131.17
Severe	Severe	Control	392.08

GSH-Px: Glutathione peroxidase

Discussion

This study measured serum GSH-Px levels before and after treatment in a study group with CoQ10 supplementation and a control group. In the study group, levels significantly increased ($P < 0.001$; Wilcoxon test). These results are similar to those of studies conducted by Hormozi in Iran in 2018. Supplementation with CoQ10 has an important role in preventing lipid peroxidation and protecting tissue against oxidative damage. In fact, by scavenging ROS, CoQ10 can be indirectly involved in regulating gene expression and modulating the activities of most enzymes. Thus, this antioxidant may alter the activity of many enzymes, especially oxidative damage repair enzymes.[17] In the control group, serum GSH-Px levels also significantly increased ($P < 0.001$; Wilcoxon Test). The skin synthesizes hydrogen peroxide to fight acne inflammation, and this can continue for several weeks until the inflammation resolves. The primary natural defense against free radicals is the prevention of their formation by various enzymes, especially GSH-Px, which regulates hydrogen peroxide levels by catalyzing the dismutation of H_2O_2 to $H_2O + CO_2$. Thus, the serum GSH-Px level increase in the control group may be due to the progress of inflammation in the pathogenesis of the disease.[18]

This study also assessed the severity of AV based on Lehmann criteria scoring. The change in severity in the study group was significant ($P = 0.008$; McNemar test). CoQ10, as an antioxidant, is essential for ATP synthesis. CoQ10 supplementation decreases lipid peroxidation by increasing antioxidant ability and removing free radicals.[19]

Statistical test results from this study showed that differences in serum GSH-Px levels based on the severity of AV before treatment were not significant ($P = 0.7$; Kruskal–Wallis test). The difference in levels based on the severity of AV after treatment was also not significant ($P = 0.3$; Kruskal–Wallis test). This result is similar to those of Aybey *et al*. in 2005, who found no significant difference in serum GSH-Px levels by the severity of AV.[20]

Conclusion

CoQ10 supplementation as an adjuvant therapy for AV can increase serum GSH-Px levels and improve the severity of AV, but there is no relationship between serum GSH-Px levels and the severity of AV.

Recommendation

Future studies are necessary for understanding the relationships between GSH-Px and other antioxidant enzymes such as SOD, CAT, and MDA as indicators of oxidative stress. Air pollution and pro-inflammatory factors may improve our ability to develop interventions to decrease oxidative stress.

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Conflicts of interest
There are no conflicts of interest.

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