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Clinical and Anti-Oxidant Effect of Adding CoQ10 to Biological Therapy in Treating Moderate to Severe Psoriasis

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ABSTRACT

Aims Psoriasis is a complex, chronic, immune-mediated, and hereditary skin disease. The present study attempted to determine whether adding CoQ10 to biological therapy can help relieve inflammation in Iraqi patients suffering from moderate to severe psoriasis.

Materials & Methods A prospective, double-blind clinical trial took place in the Department of Dermatology at Merjan Teaching Hospital in Babylon, Iraq, over three months from August to November 2021. 30 individuals from 17 to 72 years old with persistent plaque psoriasis who met the criteria for biological therapy were selected by the available sampling method. Participants were allocated into two groups (each 15 members); Group A was treated with Adalimumab + placebo (corn starch), and Group B was treated with Adalimumab + 100mg CoQ10 adjuvant. The Psoriasis Area and Severity Index (PASI) score was utilized. The sera were utilized to calculate the human superoxide dismutase and malondialdehyde via the ELISA technique.

Findings When compared to the patients before treatment, the two groups showed a substantial decline ($p<0.05$) after treatment; However, group B, which added CoQ10 to biological treatment, showed a highly significant decrease ($p<0.05$) in mean SOD level and MDA after treatment. Furthermore, following twelve weeks of treatment, group B's use of combined adjuvant therapy showed even greater recovery, as indicated by a 79% PIC PASI score improvement instead of a 60% PIC score.

Conclusion Daily administration of 100mg CoQ10 supplements to psoriatic subjects for 12 weeks has beneficial effects on reducing oxidative stress.

Keywords Psoriasis; Oxidative Stress; CoQ10; Adalimumab; Anti-Oxidant

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Introduction

Oxidative imbalance is documented in psoriasis disease; the damage to keratinocytes caused by ROS exposure results in the release of pro-inflammatory mediators and the recruitment of cellular immunity [1, 2]. Coenzyme Q10 (ubiquinone or CoQ10) is a fat-soluble vitamin-like quinone, usually called ubiquinone. It has two forms: 1) Oxidized form, which plays the role of electron carrier in mitochondrial respiration; 2) Reduced form, an endogenous antioxidant [3]. The current study presents CoQ10 as an adjuvant therapy with adalimumab. Various studies have implied that higher oxidative stress plays a part in psoriasis pathogenesis [4]. When the oxidative stress overcomes the skin's anti-oxidative ability, a change in the cellular homeostasis of the microenvironment occurs, leading to the pathogenesis of psoriasis [5].

Human skin is vulnerable to oxidative stress since it can be affected by environmental factors such as infection, skin trauma, and oxidant drugs, leading to the production of ROS/RNS, which alters DNA, protein, and lipids, resulting in the activation of NF-kB and mitogen-activated protein kinase (MAP kinase). As a result, Th1 and Th17 cells are activated, producing pro-inflammatory cytokines, which causes hyper-proliferation of keratinocytes and vascular permeability via lipid peroxidation [6]. Hyper-proliferation of keratinocytes, infiltration of the skin by immune cells, and alterations in blood vessels' permeability result from the secretion of pro-inflammatory cytokines. Thus, antioxidant supplementation may be a therapeutic target for psoriasis [7].

ROS are secondary products of cellular respiration and the folding of proteins. Also, they are the end products of several metabolic reactions. Additionally, the cells of mammals have diverse antioxidant defenses, such as superoxide dismutase (SOD), catalase, glutathione (GSH) peroxidases, as well as small molecules, namely, vitamin E, Coenzyme Q10, and selenium [8]. Previous studies found low levels of total antioxidant capacity (TAC) due to reduced activity of major antioxidant enzymes like SOD and higher tissue levels of Malondialdehyde (MDA) in psoriasis skin lesions. This confirms that oxidative stress could be important in psoriasis pathogenesis [9-11]. While serious oxidative stress leads to cell senescence and may result in the death of cells, slight oxidative stress could enhance cell survival during gene expression and protein posttranslational process [12].

Coenzyme Q10 (ubiquinone) is an endogenous lipid-soluble benzoquinone compound that functions to move electrons to complex III from complexes I and II in the inner mitochondrial membrane electron transferring system. Also, it has an important role in maintaining bioenergy homeostasis in mitochondria. Regarding chronic diseases whose pathogenesis is associated with oxidative stress (OS), CoQ10 is thought to be a likely candidate for adjunctive therapy [13]. The pathophysiology of psoriasis is associated with increased ROS production, which is induced by both Th1 and Th17 cytokines [14].

CoQ10 exists in two forms; ubiquinone (oxidized form) and ubiquinol (reduced form) that the second is dominant in the body. Regarding the source of CoQ10, the body gets one-half of its CoQ10 from food, and the remaining is endogenous. The daily requirement is approximately 500mg, and consumption of 200 mg two times in one day is needed to reach a therapeutic amount in the blood level >2.5µg/ml [15]. CoQ10 has a vital effect on organ metabolism and functions. It functions as an antioxidant in cell membranes and lipoproteins, thereby protecting cells from the possibly damaging implications of toxic free radical species created during normal cellular metabolism (oxidative stress) [16-20]. In circulation, CoQ10 could affect the production of cytokines and interleukins and modify the production of prostaglandin and leukotriene metabolites [19].

CoQ10 supplementation enhances the inflammatory state in patients with metabolic disease and rheumatoid arthritis by significantly reducing pro-inflammatory markers IL6, TNF-α, and CRP. It also reduces MDA levels, a biomarker for oxidative stress, leading to enhanced glucose control and liver function through induction of Sirt1/Nrf2 gene expression [21-24]. CoQ10 was used for supplementation, and the results indicate that it protects cells and is efficacious in treating cardiovascular diseases and obesity. Furthermore, several research papers that suggested using it as adjuvant therapy have exhibited its anti-inflammatory and antioxidant influences and its influence on mitochondrial dysfunction, which is associated with the inflammatory response [25, 26].

The present study attempted to determine whether adding CoQ10 to biological therapy can help relieve inflammation in Iraqi patients suffering from moderate to severe psoriasis.

Materials and Methods

A prospective, double-blind clinical trial took place in the Department of Dermatology at Merjan Teaching Hospital in Babylon, Iraq, over three months from August to November 2021. According to similar studies, 30 individuals from 17 to 72 years old with persistent plaque psoriasis who met the criteria for biological therapy were selected by the available sampling method. Participants were allocated into two groups (each 15 members); Group A was treated with Adalimumab + placebo (corn starch), and Group B was treated with Adalimumab + 100mg CoQ10 adjuvant.

The Psoriasis Area and Severity Index (PASI) score [4, 10, 13-15] was utilized to determine the severity of each

patient's condition through a clinical assessment conducted by the same dermatologist.

The sera were utilized to calculate the human superoxide dismutase and malondialdehyde via the ELISA technique using the appropriate ELISA kit to carry out each test before and after therapy.

Findings

The mean age of group A participants was 47.69±12.61 for males (n=13) and 48.00±9.89 for females (n=2), and group B was 42.58±12.55 for males (n=12) and 30.33±17.89 for females (n=3).

All psoriatic patients had high PASI scores before enrollment in the training (zero time). PASI score was significantly lower in group A and showed about 60% improvement change (PIC) after twelve weeks of therapy ($p<0.05$). Further improvement was reported by group B using combination adjuvant therapy of CoQ10 with Adalimumab, which dropped the PASI score from pre-treatment values by 79% PIC ($p<0.05$).

The SOD mean shows a significant increase ($p<0.05$) after treatment in both groups. Also, the reduction was significant ($p<0.001$) in the serum levels of MDA in both groups (Table 1).

Table 1. Comparing the mean of serum MDA and SOD between the therapy stage in both groups

Parameter	Pre-test	Post-test	p-Value
MDA			
Group A	9.01±1.03	5.54±0.55	0.0001
Group B	7.58±0.55	4.35±0.38	0.0001
SOD			
Group A	236.40±7.59	418.11±54.91	0.017
Group B	250.74±32.29	456.72±56.63	0.0001

Discussion

Oxidative stress is an important factor in the pathogenesis of psoriasis, as reactive oxygen species have a major impact on cell production, differentiation, and death, comprising human keratinocytes and fibroblasts [27-29]. In addition, they destroy many biomolecules in specific processes, including the secretion of pro-inflammatory cytokines or lipid peroxidation, all due to the overproduction of free radicals that can damage proteins, DNA, and lipids [30]. Malondialdehyde, which is an end product of lipid peroxidation and acts as a pro-oxidant, triggering an increase in the oxidative burden of psoriasis skin, is found to be elevated in patients with psoriasis by many studies [31-34]. On the other hand, certain enzymes that form a line of protection against oxidative stress, such as glutathione peroxidase, superoxide dismutase, and catalase, were represented to be decreased in their concentration in psoriatic patients [9, 35-38].

Using the studied treatment protocols for the psoriatic groups resulted in a highly significant reduction in MDA levels from its baseline state, and the percentage of reduction was comparable for all studied groups, although group B using metformin and CoQ10 adjuvant therapy with adalimumab resulted in a higher percentage of 63%. On the other hand, the result of this study showed that SOD levels increased significantly for the two studied groups after therapy periods, and the increment was highly significant using adjuvant therapy in group B, as related to group A using adalimumab alone. It's well documented that oxidative stress can stimulate inflammation through numerous signaling pathways comprising NF-kB, MAPK, and STAT3 [39]. MAPKS represents a family of serine/threonine protein kinases, including several membrane extra-cellular signal-regulated kinases (ERKs), c-Jun N-terminal kinases (JNKs), and p38 MAPK [40]. As ROS increases, there will be an improvement in the anti-oxidant potential, and this will induce the activation of NF-KB; this was reported by studies that showed elevated levels of p38 MAPK and ERK1/2psoriatic skin [41-43]. Such prolonged inflammatory activation through ROS will increase the release of IL-23IL-17, a key mediator cytokine in psoriasis. On the other hand, ROS produces tissue damage. It will act as a chemo-attracted substance to neutrophils and other inflammatory cells to further sustain the inflammatory state and provoke more ROS production [43]. Biological therapy represents progress in the treatment of psoriasis. Barygina *et al.* [44] studied the effect of using infliximab treatment on MDA paling level for six months and showed a decreased level of MDA after treatment [45]. Other studies using etanercept for 24 weeks reported significant improvement in the TAC [46]. Another study using an anti-CD11a IgG1 antibody, Efalizumab, weekly for 12 weeks also reports improvement in the TAC. No follow-up study links treatment with adalimumab with the level of oxidative stress markers in psoriasis yet. Beyazit *et al.* [47] report that adalimumab therapy in rats attenuated ischemia/reperfusion (I/R)-induced ovarian injury could suppress the inflammatory state, inhibit the oxidative stress, or alter the apoptotic pathway.

Also, Börcek *et al.* [48] reported a significant reduction in MDA levels in the serum of rats with induced spinal cord treatment after adalimumab treatment. Concerning the effect of adalimumab treatment on SOD level, De La Cámara *et al.* [49] and her coworkers reported that treatment with adalimumab restoring TAC and SOD activity and reduces photoreceptor cell death in a mouse model of retinal degeneration, such study suggest a beneficial role of adalimumab in restoring SOD activity [50].

Using CoQ10, which has documented antioxidant properties as it can neutralize free radicals and reduce or prevent the damage caused by ROS, improve energy, and augment the immune response, results in an additional beneficial effect in reducing MDA level and restoring CAT enzyme activity [20]. The mechanism of CoQ10 as an antioxidant is that it acts as an electron transpolar for the production of ATP inside the mitochondria. In addition, the reduced

formula of CoQ10, ubiquinol, is the active anti-oxidant agent that protects the biological membrane against oxidation and inhibits lipid peroxidation.

Conclusion

Daily administration of 100mg CoQ10 supplements to psoriatic subjects for 12 weeks has beneficial effects on reducing oxidative stress related to psoriasis and decreasing the severity of psoriasis during this period.

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