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Efficacy of antioxidants in the management of psoriasis: A case control study

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Abstract

Introduction: Psoriasis is a chronic, immune-mediated inflammatory dermatosis. The pathophysiology of the disease is still incompletely elucidated and multiple factors are said to be involved in its initiation and perpetuation, e.g., stressors, genetic factors, environmental factors. In the last decade, a new theory is trying to explain the pathophysiology of this disease by looking at the role played by oxidative stress and chronic inflammation in the initiation of keratinocyte proliferation and differentiation. Keeping in consideration the increased oxidative stress in the patients of psoriasis, the anti-oxidant drugs can form an important part of the therapeutic ladder of psoriasis.

Materials and Methods: The aim of this study was to measure the possible role of oxidative stress in psoriasis patient by measuring SOD level and comparing it with normal individuals and administer antioxidants supplements to the patients group to see the efficacy. It was a Case- Control study (1st part) and Clinical Trial without control group (2nd part). The study was carried out in Psoriasis awareness Club from June 2023 to December 2023. Purposive sampling done who fulfill the inclusion & exclusion criteria. 23 patients with psoriasis and 23 age and sex matched control subjects were recruited for this study. Clinical severity of the disease was determined by PASI score. All patients and control subjects were examined for plasma SOD level. 23 psoriatic patients were given antioxidant therapy in the form of once daily tablet for 30 days. PASI score, DLQI and SOD (Superoxide dismutase) level were measured before therapy (day 0) and after therapy (day 30) in patients group.

Statistical analysis and Results: Data were expressed as mean ± standard deviation (SD) for quantitative variables and numbers. For comparison of two means (t test) and (ANOVA "F") test were used for several means. Chi-square ($\chi 2$) or fisher exact test were used when appropriate, ($P<0.05$) was considered statistically significant. The mean age of the patients and control subjects were 37.64 (±5.89) and 33.6 (11.02) years, respectively. The mean duration of the disease was 12.43 (±8) years. No significant difference was observed between SOD level of psoriatic patients & controls. No significant correlations of SOD level with severity of psoriasis and duration of disease were found. We observed no statistically significant difference in PASI and DLQI scores before and after antioxidant therapy but there was significant increase in the level of SOD after treatment.

Conclusion: It is indisputable that antioxidant supplementation can reduce the overall morbidity, enhance the prognosis of psoriasis. Notably, in most cases, antioxidants alone are not able to induce significant clinical changes in the aspect and/or course of the disease, except perhaps in mild forms. They must be used in conjunction with standard pharmacological treatments to achieve measurable results.

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Keywords: Antioxidant; Efficacy; Psoriasis; Management

1. Introduction

Psoriasis is a chronic, immune-mediated inflammatory dermatosis characterized by the appearance of erythematous plaques, covered by white scales, occasionally pruritogenic, and distributed mainly on the extensor areas (elbows, knees, scalp, chest). [1] Its prevalence varies from 0–2.1% in the pediatric population to 0.91–8.5% in adults. Psoriasis is a debilitating condition, which significantly affects the quality of life and impacts on the life expectancy of individuals who suffer from it. [2] The pathophysiology of the disease is still incompletely elucidated and multiple factors are said to be involved in its initiation and perpetuation, e.g., stressors, genetic factors, environmental factors. [3] In the last decade, a new theory is trying to explain the pathophysiology of this condition by looking at the role played by oxidative stress and chronic inflammation in the initiation of keratinocyte proliferation and differentiation that underline psoriasis. [4]

Oxidative stress is defined as an imbalance or a transient or chronic increase in the levels of free oxygen/nitrogen radicals, either as a result of the exaggerated elevation in their production or the decrease in their ability to be eliminated by antioxidant systems. [5] Due to its role as a barrier and its direct exposure to environmental factors, the skin is an important source of free radicals that play, when in low concentrations, an essential role in the defense against microorganisms and in cell differentiation[6]. When their concentration increases, leading to oxidative stress, free radicals appear to be involved in DNA alteration, cell protein degradation, lipid oxidation, apoptosis, tissue injury, altered response of T-helper cells and secretion of interleukin-17 (IL-17). As all these are essential stages in the initiation and perpetuation of psoriasis, the hypothesis that oxidative stress plays a key role in the pathophysiology of this chronic dermatosis has emerged. [2]

Oxidative stress mainly resulting from oxidant/antioxidant imbalance. Malondialdehyde (MDA), a byproduct of lipid peroxidation, increases and works as a pro-oxidant, exacerbating the oxidative load on psoriatic skin. On the other hand, certain enzymes including glutathione peroxidase (GP), superoxide dismutase (SOD) and catalase (CAT) act as antioxidants and form an important line of defense which decrease the concentration of the most harmful oxidants and help in maintaining equilibrium between the production and destruction of the reactive oxygen species (ROS) in the body. In patients of psoriasis, imbalance is seen in this equilibrium which may manifest as either excessive production of ROS or decrease in anti-oxidants. [7]

The antioxidant enzyme family of superoxide dismutase (SODs) is considered to be the first line of defense against oxygen toxicity. These metalloenzymes act to dismute toxic superoxide radicals to oxygen and hydrogen peroxide. It has been suggested that increased generation of superoxide anion radicals from neutrophils and neutrophil accumulation in psoriatic lesions may cause abundant superoxide production during the phagocytic reaction and systemic activation of circulating neutrophils in psoriatic patients. As a result of insufficient antioxidant mechanisms, there is increased accumulation of ROS during the inflammatory process in psoriasis results in cascade of reactions which are responsible for epidermal hyperproliferation. [8]

Psoriasis is not completely curable which is why the search for new effective therapies is a highly relevant area of research. To identify new therapeutic compounds, the first step is to study the role of various factors underlying the development of psoriasis. One such factor is oxidative stress. Keeping in consideration the increased oxidative stress in the patients of psoriasis, the anti-oxidant drugs can form an important part of the therapeutic ladder of psoriasis.

For this purpose we aimed to measure the possible role of oxidative stress in psoriasis patient by measuring SOD level and comparing it with normal individuals & administer antioxidants supplements to the patients group to see the efficacy.

2. Material and methods

The aim of this study was to measure the possible role of oxidative stress in psoriasis patient by measuring SOD level and comparing it with normal individuals and administer antioxidants supplements to the patients group to see the efficacy.

It was a Case- Control study (1st part) & Clinical Trial without control group (2nd part). The study was carried out in Psoriasis awareness Club from July 2023 to December 2023. The selection criteria and protocol were approved by the local Institutional Review Board (IRB). Group A consists of 23 subjects of psoriasis while group B, 23 healthy age and sex matched individuals from the general population without any previous history of psoriasis. Proforma was duly

filled and written consent was taken in all the cases. Thorough history was taken and complete clinical examination was performed. Purposive sampling done who fulfill the inclusion & exclusion criteria. Inclusion criteria included diagnosed case of psoriasis, age>18 years, Mild to Moderate cases. Patients were diagnosed clinically by dermatologist and when required histopathologically. Exclusion criteria included conditions that could affect the redox state such as obesity, smoking and diseases such as anaemia, diabetes mellitus, cardiovascular diseases, liver or kidney diseases and inflammatory skin diseases. Pregnant & lactating women, psoriatic patients with any topical therapy or systemic antioxidant therapy within 4 weeks or systemic drug therapy or photochemotherapy within 3months were excluded from the study. Clinical severity of psoriasis was determined by Psoriasis Area Severity Index (PASI) score. All patients & control subjects were examined for plasma SOD level. 23 psoriatic patients were given antioxidant therapy in the form of once daily tablet for 30 days . PASI score, DLQI and SOD level were measured before therapy (day 0) and after therapy (day 30) in patients group.

Active Ingredients of antioxidant:

- Cucumis Melo L (Melon Extract/Extramel-M) 10 mg,
- Vitamin E 10 mg,
- Vitamin C 40 mg,
- Vitamin B9 (Folic Acid) 100 µg,
- Vitamin B12 (Cobalamin) 1 µg,
- Copper Gluconate 1 mg,
- Selenium 40 µg,
- Zinc Gluconate 5 mg.

Primary antioxidants (SOD) from melon extract which inhibits the production of both main cellular oxidants superoxide radical and hydrogen peroxide. Vitamins & minerals act as secondary anti-oxidants.

Measured the SOD in each sample by ELISA kits based on WST-8 method. The WST -8 method is based on the colorimetric reaction WST-8.

2.1. Statistical analysis

Data were checked, entered and analyzed by using Microsoft Excel software computer package. Data were expressed as mean ± standard deviation (SD) for quantitative variables, number. For comparison of two means (t test) and (ANOVA "F") test were used for several means. Chi-square ($\chi 2$) or fisher exact test were used when appropriate, ($P<0.05$) was considered statistically significant.

3. Results

The study included 23 patients with psoriasis (13 males and 10 females) and 23 age-and sex- matched healthy subjects as a control group (14 males and 9 females). The mean age of the patients and control subjects were 37.64 (±5.89) and 33.6 (11.02) years, respectively. The mean duration of the disease was 12.43 (±8) years.

Table 1 Demographic Characteristics of the patients with psoriasis and healthy subjects

	Control	**Psoriasis Patients**
Age Mean ± SD	37.64 ± 5.89	33.6 ± 11.02
Gender M/F	13/10	14/9
Duration of disease		12.43 ± 8

Plasma SOD levels showed slight decrease in psoriatic patients with mean and standard deviation 32.67 and 12.11 compared to control subjects with mean and standard deviation 39.7 and 12.4 ($P = 0.115$) (Table: 02). But the difference was not statistically significant.

Table 2 SOD levels in patients Vs Healthy Controls

	Cases (n=23)	**Control (n = 23)**	**P**	**Significance**
SOD (range) mean ± SD	(10.5-53.62) 32.67± 12.11	(24-64) 39.7 ± 12.14	0.115	NS

Table 3 Correlation of SOD levels with severity of psoriasis

	Mild Psoriasis n= 19	**Moderate psoriasis (n=4)**	**p**	**Significance**
SOD (range) mean ± SD	(17-53.62) 33.42 ± 12.15	(25.7-43) 34.35± 14.14	0.929	NS

As regard correlations with severity of psoriasis, there was no significant correlations with SOD and Severity of Psoriasis. (P > 0.05). **(Table: 03)**

Table 4 Correlation in between the duration of psoriasis and the level of SOD in psoriasis patients

	r	**p**	**Significance**
SOD	0.2107	0.334	NS

There were insignificant correlations between the duration of the disease and the levels SOD with r value of 0.2107 and (P > 0.05) (Table 4).

Table 5 Mean SOD level before and after treatment

	Before treatment	**After Treatment**	**p**	**Significance**
SOD (range) mean +SD	(10.5-53.62)4.63+ 2.26	(15-55), 5.54+ 2.8	0.0002	Significant

(Table: 5) There was significant statistical difference in the level of SOD before treatment having mean ± Standard deviation 4.63± 2.26 and after treatment with mean and standard deviation 5.54± 2.8 (p<0.5).

Table 6 Changes in PASI, DLQI score and SOD levels after antioxidant therapy

	Before treatment	**After treatment**	**p value**	**Significance**
PASI (range) mean ± SD	(1.3-11.4) 5.54 ± 2.8	(1.5-10) 4.63 ± 2.26	0.226	NS
DLQI (range) mean ± SD	(3-9)5.58 ± 1.38	(3-6)4.31 ± 0.9	0.99	NS
SOD (range) mean ± SD	(10.5-53.62)4.63± 2.26	(15-55),5.54± 2.8	0.0002	Significant

There was non-significant statistical difference in PASI score and DLQI score (p>0.05) before and after treatment with antioxidant therapy, but significant difference of SOD level between before and after treatment (p<0.05) with antioxidant therapy (Table 6).

4. Discussion

There is compelling evidence that ROS-mediated oxidative stress is involved in a vast number of biological responses causing DNA modification, lipid peroxidation, and production of inflammatory cytokines which could contribute to the pathogenesis of many inflammatory skin diseases, including psoriasis. [9]

In most papers delineated a significant alteration of the redox balance, with a significant decrease in antioxidant enzymes i.e., superoxide dismutase and glutathione peroxidase in psoriasis patients with variable duration of the disease and an increase in pro-oxidant molecules in psoriasis. [1]

However, Few studies have investigated the role of oxidants / antioxidants systems in psoriasis with discordant results (Hussain et al., 2014).[10]

Antioxidants are classified as either non-enzymatic or enzymatic. The first group includes exogenous non-enzymatic molecules such as vitamins E, A, and C, flavonoids, carotenoids, plant polyphenols, theaflavin, allyl sulfides, selenium, and curcumin. Endogenous non-enzymatic molecules include melatonin, bilirubin, uric acid, polyamines, and glutathione (GSH). GSH belongs to the glutathione system, which includes the enzymes glutathione reductase, glutathione peroxidase (GPX), and glutathione-S-transferase (GST). Enzymatic antioxidants also include superoxide dismutase (SOD), superoxide reductase, CAT, and thioredoxin. [11]

SOD, an antioxidant enzyme accelerates the dismutation of the toxic superoxide radicals produced during the oxidative energy processes into the less harmful molecules, hydrogen peroxide and molecular oxygen. The significant decrease in the levels antioxidant (SOD) may be a reflection of oxidative stress caused by consumption of SOD in the process of detoxification of superoxide radicals.

In the pre-diagnostic stage, serum antioxidants are low because they have been used in reducing inflammatory products. Decreased SOD activity might be related to epidermal hyper proliferation, because the ROS are thought to induce cell proliferation in various cell systems. Decreased SOD activity could be caused by increased superoxide anion production during the psoriatic process in the skin as well as activated peripheral neutrophils article.

A conundrum of research endeavors which collected venous blood samples from individuals suffering from psoriasis with variable duration of the disease detected low levels of total antioxidant status and alterations in enzymes involved in decreasing free oxygen radicals concentrations, i.e., catalase, superoxide dismutase, paraoxonase-1 and glutathione peroxidase.[1]

Gabr SA et al,2012[12] found that serum SOD activities were significantly decreased in all severity psoriatic patients as compared with healthy controls. Lowest SOD level was found in severe psoriasis group.

In another study by Abdel-Mawla MY et al.,2013 found SOD levels were significantly lower in psoriatic patients than in controls and SOD levels decreased with increased severity of the disease.[9]

In the present study, though we found decrease level of SOD in patients group compared to healthy individuals but it didn't show statistical significance.

Several studies with contradictory results were also present, highlighting that in psoriasis a significant elevation in the levels of the aforementioned antioxidant molecules can also occur. It may be hypothesized that, in psoriasis, there is a compensatory increase in antioxidant systems in order to counterbalance the elevated levels of oxidative stress.

The disease duration may play a significant role in the severity of disease increasing both abnormal immune reactions and oxidative free radicals. Oxidative stress markers share an association with the duration and severity of the disease. The correlation between the severity of psoriasis and antioxidant status is controversial. In previous studies by Gabr SA et al,2012 [12] and Abdel-Mawla MY et al.,2013 [9] found negative correlation of SOD level with PASI score. Hussain et al.[10], 2014 demonstrated no statistically significant correlation between the PASI score and the plasma SOD level. Baz et al.,2003.[17]found no correlation between the PASI score and oxidative stress in patients with psoriasis. Many studies did not find significant correlations between oxidative stress parameters and the severity or the duration of psoriasis. [1] However, no significant correlation was found between the levels SOD and severity of psoriasis (PASI) in our study as observed in some of the previous investigations.

Similar results were obtained by Kaur et al.[7] who reported that in psoriasis, oxidative stress markers do not correlate with age, disease duration or severity, despite the fact that there are notable alterations of the redox balance, i.e., increased oxidative markers and decreased antioxidant system. In a study by Abdel-Mawla MY et al.,2013 [9] included 34 patients psoriasis and 30 age-and sex- matched healthy subjects as a control group showed insignificant correlations between the duration of the disease and the levels SOD similar to our study.

Several antioxidants are potentially being considered as potential therapies for psoriasis in combination with drugs that have proven efficacy. Wolters (2005), [13] his study on psoriasis explored that the antioxidant supplementation in the treatment of psoriasis is proved beneficial. In the report of Kharaevea et al., (2009),[14] 58 patients with erythrodermic psoriasis and psoriatic arthropathy showed significant clinical improvement and reduction of oxidative stress after 5

weeks treatment with conventional therapy plus supplementation with antioxidant therapy in the form of coenzyme Q10, vitamin E and selenium.

Madhulatha and Vijayabhaskar (2019)[15] reported antioxidant supplementation therapy along with conventional therapy for 8 weeks, in psoriatic patients, resulted in a significant decrease in mean serum levels of MDA, while the total antioxidant levels increased significantly. Relhan et al.,2002 [16]in their study observed the same results. With exception, Abdel-Mawla MY et al.,2013 [9] reported no changes in PASI score, levels of SOD before and after antioxidant therapy. Our study showed significant change in SOD level after antioxidant therapy

5. Conclusion

To date, only a few studies have investigated the effect of antioxidant supplementation in psoriatic cases. The hypothesis of an imbalance between oxidants and antioxidants in psoriasis and its role in the pathogenesis of the disease and efficacy of antioxidants in psoriasis should be further investigated. It is indisputable that antioxidant supplementation can reduce the overall morbidity, enhance the prognosis of psoriasis. Notably, in most cases, antioxidants alone are not able to induce significant clinical changes in the aspect and/or course of the disease, except perhaps in mild forms. They must be used in conjunction with standard pharmacological treatments to achieve measurable results. Combinations of antioxidant treatments seem to be more effective by exploiting the synergistic effect of the various molecules, which act differently on oxidative stress.

Compliance with ethical standards

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Limitation

Small number of patients may explain the negative results. All oxidative markers were not possible to evaluate due to lack of Lab facilities. Longer duration of antioxidants, use of other types of antioxidants in larger number of psoriasis patients might have explored a better potential therapeutic efficacy of antioxidants in psoriasis therapy.

Disclosure of conflict of interest

Uni-Health and Uni-Derma pharmaceutical, for supporting with medication and laboratory support.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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