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Role of Lipid Peroxidation Product as a Marker of Oxidative Stress in Patients with Psoriasis

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Abstract **Original Research Article**

This was a prospective descriptive type study conducted in the Department of Pharmacology and Therapeutics in collaboration with the Department of Dermatology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh during the period from July 2014 to June 2015. The aim of the study was to measure the lipid peroxidation product malondialdehyde (MDA) as a marker of oxidative stress in psoriasis patients in the treatment process. Psoriasis is a chronic inflammatory, proliferative skin disease considered as compulsive skin lesions due to various exogenous and endogenous factors. It is associated with a number of biochemical and immunological disturbances. A total of 26 clinically diagnosed psoriasis patients were included in this study. Clinically diagnosed psoriasis patients of both sexes who came for first treatment purposes in Dermatology OPD of Rajshahi Medical college hospital were included in this study. Newly diagnosed psoriatic patients who fulfilled the inclusion criteria were also included in this study. The data was expressed as mean ± standard deviation. Paired t- test was employed for the statistical analysis of data. P- value less than 0.05 was taken as significant. Pre-treatment the MDA level of 15 clinically diagnosed mild psoriasis patients was 3.00±0.45 µmol/l which was decreased to 2.83±0.52 µmol/l after conventional treatment with topical corticosteroid and oral vitamin A for one month. This decreased level was statistically highly significant (P<.001). Post-treatment, the MDA level of 11 clinically diagnosed severe psoriasis patients was 3.89±1.17 µmol/l which was decreased to 2.50±1.03 µmol/l after conventional treatment with oral methotrexate, vitamin A and topical corticosteroid for one month. This decreased level was statistically highly significant (P<.001).From the reflection and outcomes of the present study, it is revealed that after conventional treatment for one month showed the plasma MDA level which is the product of lipid peroxidation was decreased significantly. So, it can be focused that conventional treatment decreases the lipid peroxidation as well as oxidative stress.

Keywords: Lipid Peroxidation, Psoriasis, Oxidative Stress.

INTRODUCTION

Psoriasis is a common chronic, inflammatory, proliferative skin disease that mostly presents as chronic sharply demarcated, dull red, scaly plaques, particularly on extensor prominences and the scalp 'Psoriasis' [1]. Psoriasis is a chronic inflammatory skin disease characterized by a noticeable increase in keratinocyte proliferation, anomalous change of keratinocytes, prominent variations in dermal capillary vasculature and existence of dermal and epidermal mononuclear leukocytes and neutrophils [2]. Several studies over the years consume implicated the role of increased oxidative stress in the pathogenesis of psoriasis. After the oxidative stress overwhelms the anti-oxidant capacity of the skin, it leads to a modification of cellular homeostasis which alters the phenotype creating a microenvironment beneficial to the expansion of disease processes. There is increase in malondialdehyde (MDA) which stays an end product of lipid peroxidation and acts as a pro-oxidant causing increase in oxidative burden of psoriatic skin [3]. However, in psoriasis, the normal cycle of replacing old skin cells with new one becomes unbalanced [4]. The skin is a potential target for oxidative injury, as it is

continuously exposed to UV (Ultraviolet) radiation and other environmental stresses generating free radicals or reactive oxygen species (ROS). Free radicals are chemical species that have a single unpaired electron in an outer orbit. Free radicals initiate autocatalytic reactions, whereby molecules with which they react are themselves converted into free radicals, thus propagating the chain of damage. The increased generation of ROS might target cellular polyunsaturated fatty acids for lipid peroxidation. Increased lipid peroxidation is indicated by increased concentration of malondialdehyde (MDA) in serum of psoriasis patients. MDA is an organic compound which is very reactive towards proteins, with which they form a wide range of inter and intramolecular adducts [5]. The production of this aldehyde is used as a biomarker to measure oxidative stress in an organism [6]. Several evidences suggest that ROS and oxidative stress are involved in the pathogenesis of psoriasis [7, 8]. ROS-mediated oxidative stress is involved in a vast number of biological responses causing lipid peroxidation, DNA modification, and production of inflammatory cytokines which could contribute to the pathogenesis of psoriasis [9]. ROS produced during the inflammatory process in psoriasis from polymorphonuclear leukocytes can contribute to neutrophil activation which may play an important role in this disease process. On the other hand, patients with severe psoriasis is treated with systemic agents such as oral methotrexate (MTX), vitamin A and topical corticosteroid. Low dose methotrexate is one of the classical agents and still one of the most frequently used systemic treatment for psoriasis worldwide. MTX is a potent immune suppressant which markedly depress cytokine production and cellular immunity and has anti-inflammatory property [10]. It exerts anti-inflammatory effects mediated through intracellular accumulation of 5-aminoimidazole-4-carboxyamide ribonucleotide, thereby increasing the release of adenosine. Adenosine exerts anti-inflammatory effects mainly on neutrophils, where an inhibition of adhesion and reactive oxygen intermediate production has been demonstrated 'Psoriasis' [11]. It is believed that MTX affects oxidative stress and it decreased the plasma MDA level and increased antioxidant level in psoriasis patients [5]. All these evidences suggest that using the conventional methods possess beneficial effects in patients with mild and severe psoriasis. Though several researchers have been studied on oxidative stress in psoriasis patients pre and post treatment by conventional methods from abroad, no study have yet been done in our country regarding the status of oxidative stress in psoriasis patients Pre and post treatment with conventional method. In line to the connection of pharmacological and chemical information's obtained from different literatures, the research program has been designed to measure lipid peroxidation product MDA level Pre and post conventional treatment of psoriasis in order to determine the status of oxidative stress as well as to evaluate the given treatment schedule.

OBJECTIVES

a) General Objective

To measure the lipid peroxidation product Malondialdehyde (MDA) as a marker of oxidative stress in patients with psoriasis.

b) Specific Objectives

To evaluate the association of Malondialdehyde (MDA) with oxidative stress in psoriasis patients pre and post treatment.

METHODOLOGY AND MATERIALS

The present study was carried out in the Department of Pharmacology and Therapeutics in collaboration with the Department of Dermatology, Rajshahi Medical College Hospital, Rajshahi. A total of 26 clinically diagnosed psoriasis patients were included in this study. Newly diagnosed psoriatic patients who fulfilled the inclusion criteria were included in this study. Before starting treatment, patients were divided into two categories: mild and severe cases. After taking informed consent, complete history taking, physical examination was done and recorded in a preformed data sheet. The study protocol was taken from the Institutional Review Board of Rajshahi Medical College. Purposive sample technique was use for this study. The most frequently used test is the measurement of MDA by the thiobarbituric acid (TBA) reaction. Here, TBA reacts with MDA to form a pink 2:1 TBA: MDA adduct, which is extracted by n-butanol and absorbs maximally at 532 nm.The data was expressed as mean ± standard deviation. Paired t- test was employed for the statistical analysis of data. P- value less than 0.05 was taken as significant.

Inclusion Criteria

- Clinically diagnosed psoriasis patients in the age group of 20-60 years.
- Both genders.
- No history of any drug therapy for psoriasis for last two months.

Exclusion Criteria

- Known case of Rheumatoid arthritis, Diabetes mellitus, Coronary heart disease and Atherosclerosis.
- Smokers.
- Alcoholics.
- Persons taking antioxidant therapy.

RESULTS

A total of 26 clinically diagnosed psoriasis patients were selected for this study. Pre-treatment, the MDA level of 15 clinically diagnosed mild psoriasis patients was 3.00±0.45 µmol/l which was decreased to 2.83±0.52 µmol/l after conventional treatment with topical corticosteroid and oral vitamin A for one month. This decreased level was statistically highly significant

(P<.001) which are shown in Table-1 and Figure-1. post-treatment, the MDA level of 11 clinically diagnosed severe psoriasis patients was 3.89±1.17 µmol/l which was decreased to 2.50±1.03 µmol/l after conventional treatment with oral methotrexate, vitamin A and topical corticosteroid for one month. This decreased level was statistically highly significant (P<.001) which are shown in Table-2 and Figure-2.

Table-1: MDA level in patients of mild psoriasis pre and post conventional treatment (n= 15)

Number of patients	MDA level (µmol/l)		P value
	Before treatment (BT)	After treatment (AT)	
1	2.4	2.0	
2	3.5	2.8	
3	3.2	2.8	
4	2.7	2.7	
5	1.9	1.8	
6	3.3	3.0	
7	3.8	3.7	
8	3.2	3.5	<.001
9	2.8	2.6	
10	3.2	3.0	
11	3.0	2.8	
12	3.1	3.6	
13	3.0	2.8	
14	3.1	2.9	
15	2.8	2.5	
Mean±SD	3.00±0.45	2.83±0.52	

The significance of difference pre and post treatment was calculated using student's paired t-test.

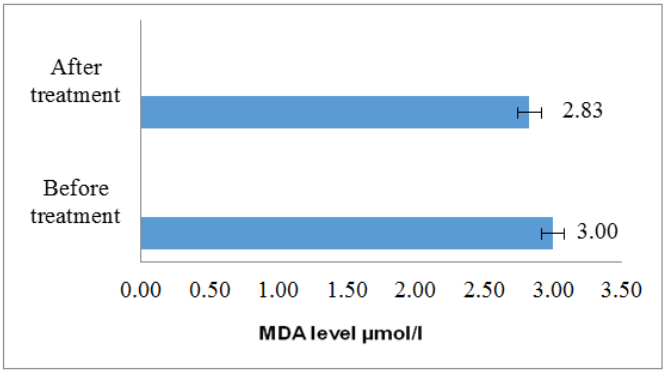

Fig-1: Bar diagram showing MDA level in mild psoriasis patients pre and post treatment (n= 15)

Table-2: MDA level in patients of severe psoriasis pre and post conventional treatment (n= 11)

Number of patients	MDA level(µmol/l)		P value
	Before treatment (BT)	After treatment (AT)	
1	4.2	1.2	<.001
2	3.0	2.2	
3	3.5	3.0	
4	3.6	2.6	
5	1.6	1.4	
6	6.0	3.8	
7	3.7	2.0	
8	3.2	1.0	
9	5.0	4.0	
10	4.0	3.2	
11	5.0	3.1	
Mean±SD	3.89±1.17	2.50±1.03	

The significance of difference pre and post treatment was calculated using student's paired t-test.

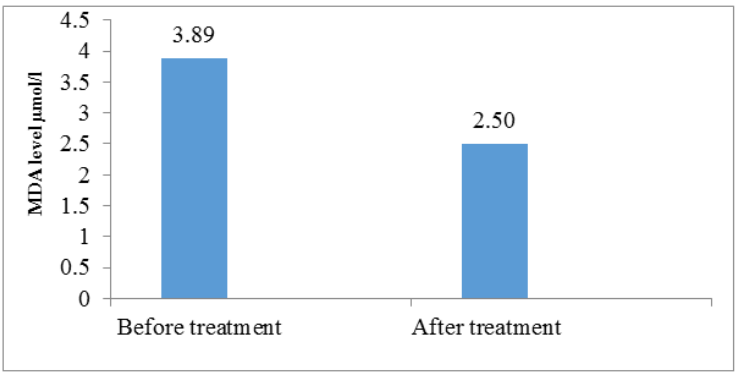

Fig-2: Bar diagram showing MDA level in severe psoriasis patients pre and post treatment (n= 11)

DISCUSSION

In the present study, the treatment profile of topical steroid & oral vitamin A were studied on the status of oxidative stress in mild psoriatic patients. On the other hand, in severe psoriatic patients, the effect of oral methotrexate, vitamin A and topical steroid were evaluated. A total number of 26 clinically diagnosed psoriatic patients of 15 mild cases and 11 with severe cases were studied. Plasma MDA level was measured before starting treatment and also after treatment with MTX, vitamin A and topical steroid for one month. Clinically, those patients were improved significantly. Those patients were also advised to take a strict dietary regimen to be followed during the treatment period (that is, avoidance of red meat and intake of fish, vegetables and fruits). In mild psoriatic patients, the pretreatment value of MDA was 3.00±0.45 µmol/l which was decreased significantly to 2.83±0.52 µmol/l after combined treatment with topical steroid and oral vitamin A for one month [12]. Showed that the topical treatment decreased plasma MDA concentration and increased glutathione peroxidase activity in erythrocyte after 20 days treatment which was not statistically significant. They suggested that the external treatment by topical betamethasone with salicylic acid, tar and cignoline caused improvement in skin state, an increase in glutathione peroxidase activity, and a decrease in MDA concentration in psoriasis patients [13] found that only topical application of betamethasone, salicylic acid, tar and cignoline for 20 days reduce the MDA level and increase SOD, CAT activity in erythrocytes of psoriasis patients. The applied topical treatment resulted in improvement of the condition of the skin, increased activity of antioxidant enzymes and reduced concentration of MDA [14]. Observed a topical improvement in skin state, normalization of the lipid content of cellular membranes, normalization of the MDA concentration in platelets, a further increase in GPx activity, and a lengthening of bleeding time after dietary supplementation of fish oil (20ml/day) for 8 weeks. A diet of fish oil stabilizes the lipid membrane structure and reduces increased platelet activity in psoriasis patients [15]. Found only antioxidant therapy in the form of selenium, vitamin A, C, E for one month decreased plasma MDA level which was not significant. They suggested that use of antioxidants for longer duration, other types of antioxidants in large number of psoriasis patients might have explored a better potential therapeutic efficacy of antioxidants in psoriasis therapy. In this study, vitamin A was given with topical steroid. Probably, the combination (topical steroid and vitamin A) showed a synergistic effect in decreasing plasma MDA and relief of oxidative stress in mild psoriatic patients. In severe psoriatic patients, the MDA level was 3.89±1.17µmol/l before treatment which was decreased significantly to 2.50±1.03 µmol/l as shown in Table-2 after treatment with oral methotrexate, vitamin A and topical steroid. The result was in conformation with the result of[5] who also found a decrease in MDA level after MTX therapy for 24 weeks which was statistically significant. They suggested the clinical efficacy of MTX seems to correlate with the decrease of the oxidative status in the MTX treated group and it also have antioxidative properties during treatment of psoriasis [16] observed that serum MDA level decreased significantly after treatment with MTX for 3 weeks. Low dose MTX in psoriasis exerts anti-inflammatory effects, inhibit the production of ROS and thereby reduces inflammatory cells induced oxidative stress. In this study probably, oxidative stress was reduced due to combined effect of MTX, vitamin A and topical steroid treatment. Therefore, the overall findings concluded that lipid peroxidation product MDA level which is a potent oxidative stress marker was decreased after treatment in both mild and severe cases.

LIMITATIONS OF THE STUDY

This was a prospective descriptive study in a single community with comparatively small number of sample size. So, the study result may not reflect the exact scenarios of the whole country.

CONCLUSION AND RECOMMENDATIONS

From the reflection and outcomes of the present study, it is revealed that after conventional treatment for one month showed the plasma MDA level was decreased significantly. So**,** it can be focused that conventional treatment decreases the lipid peroxidation as well as oxidative stress. This study provides a significant indication of considerable increase in the oxidative stress in patients of psoriasis once compared

to healthy individuals. So, attenuation of oxidative stress might remain a relevant therapeutic approach in these patients.

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