

Oxidant / Antioxidant Status in Patients with Psoriasis

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Psoriasis is a common, chronic inflammatory skin disease with unknown etiology. Recently it has been suggested that increased ROS production and deficient function of antioxidant systems activities may be involved in the pathogenesis of the disease. Although there are several studies investigating oxidant/antioxidant systems in psoriatic patients, the data obtained from these studies is not concordant. In this study, superoxide dismutase (SOD) enzyme activity, and malondialdehyde (MDA) and antioxidant potential (AOP) levels in thirty-five patients with psoriasis were investigated and compared with those of twenty-four control subjects. Clinical severity of the disease was determined according to the Psoriasis Area and Severity Index (PASI) scores in the patients. Plasma SOD activity and MDA levels were significantly higher ($p=0.012$ and $p=0.005$ respectively), whereas AOP levels were lower, in patients than controls ($p=0.001$). There was no correlation between PASI scores and plasma SOD, MDA, and AOP levels. Our findings may provide some evidence for a potential role of increased ROS production and decreased antioxidant activity in psoriasis.

Key Words: Psoriasis, malondialdehyde, superoxide dismutase, antioxidant potential, plasma

INTRODUCTION

The skin is a major target of oxidative injury due to reactive oxygen species (ROS) that originate in the environment and in the skin itself. ROS - superoxide anions, hydroxyl and hydroperoxyl radicals, hydrogen peroxide etc,- are produced during physiological and pathophysiological processes and scavenged by antioxidants. Antioxi-

dants attenuate the damaging effects of ROS and can impair and/or reverse many of the events that contribute to epidermal toxicity and disease. In normal aerobic cells, there is a balance between oxidative damage and antioxidant protection. However, inadequate antioxidant protection or excess ROS production creates a condition known as oxidative stress, contributing to the development of cutaneous diseases and disorders.^{1,2}

Psoriasis is a common, chronic inflammatory skin disease with unknown etiology.^{3,4} It has been suggested that increased ROS production and deficient function of antioxidant systems activities may be involved in the pathogenesis of the disease.^{1,2,5,6} There are several studies investigating the role of oxidant/antioxidant systems in the pathogenesis of psoriasis with discordant results.

In this study, our purpose was to investigate the oxidant/antioxidant status in psoriatic patients by measuring plasma superoxide dismutase (SOD) activity, malondialdehyde (MDA) levels, and antioxidant potential (AOP) levels and to look for a correlation between their levels and the severity of the disease.

MATERIALS AND METHODS

This study was conducted between September 2001 and November 2002 in the Dermatology Department of Mersin University School of Medicine. Thirty-five patients with psoriasis (22 women and 13 men, aged from 14 to 66 years) with a mean age of 42.54 ± 13.70 were included in the study. Twenty-four age and sex-matched healthy individuals (14 women and 10 men, between 17 and 66 years of age) with a mean age of $44.00 \pm$

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13.04 were selected as the controls.

Thirty patients had plaque, three had guttate, and two had palmoplantary type psoriasis. Disease duration ranged from 1 month to 30 years. Clinical severity of the disease was determined according to the Psoriasis Area and Severity Index (PASI) score.⁷

All patients and control subjects were examined for plasma SOD activity, and MDA and AOP levels. Both patients and controls had no history of any topical or systemic drug therapy for at least one month prior to blood collection, and none of them had any other co-existent disease. There was no difference between the patients and controls with regard to smoking or alcohol intake.

The fasting blood samples of both groups were drawn into citrate (3.5 mg/ml blood) containing glass tubes and centrifuged at $480 \times g$ for 10 minutes, and plasma samples were stored at -20°C until analysis.

MDA method was based on the spectrophotometer absorbance measurement of the pink coloured product of thiobarbituric acid-MDA complex formation and results were expressed as nmol/ml.⁸

SOD enzyme activity was measured as described previously.⁹ One unit of SOD activity was defined as the enzyme protein amount causing 50% inhibition in nitroblue tetrazolium (NBT) reduction rate and results were expressed as U/ml.

Plasma AOP was assessed as described previously,¹⁰ mainly based on the determination of MDA levels before and after exposure to superoxide radicals produced by xanthine-xanthine oxidase system. Results were expressed as $\text{nmol}^{-1}/\text{ml}\cdot\text{h}$. All procedures were performed at $+4^{\circ}\text{C}$ throughout the experiments.

Student-t test and Pearson correlation coefficient test were performed for statistical analysis.

RESULTS

In the patient group, the mean disease duration was 7.83 ± 8.14 years (range 1 month to 30 years). The mean value of PASI scores was 4.37 ± 3.12 (range 0.5 to 12.7).

The results of the plasma levels of MDA, SOD and AOP in patients and controls are summarized in Table 1.

Plasma SOD enzyme activity and MDA levels were significantly higher ($p=0.012$ and $p=0.005$ respectively), whereas AOP levels were lower, in patients than in controls ($p=0.001$) with student-t test (Table 1). There were no statistically significant correlations between PASI scores and plasma levels of SOD ($r=0.134$, $p=0.451$), MDA ($r=-0.121$, $p=0.503$) or AOP ($r=-0.033$ and $p=0.853$) in the patient group.

DISCUSSION

Psoriasis is a common, chronic inflammatory skin disease characterized by a marked increase in keratinocyte proliferation, abnormal differentiation of keratinocytes, prominent alterations in dermal capillary vasculature and the presence of dermal and epidermal mononuclear leucocytes and neutrophils.^{3,4} Increased capacity for chemotaxis and adhesion,^{3,5} and increased ROS production in neutrophils¹¹ have been reported in patients with psoriasis. It has also been suggested that generation of ROS from neutrophils,¹¹ keratinocytes,¹² and fibroblasts¹³ can contribute to neutrophil activation, which plays an important role in psoriatic process. This evidence supports the view that ROS may play a role in the pathogenesis of psoriasis.^{1,2,5,6} Increased ROS production during the inflammatory process in psoriasis, as a result of insufficient antioxidant mechanisms,

Table 1. Plasma Malondialdehyde (MDA), Superoxide Dismutase (SOD) and Antioxidant Potential (AOP) Levels (mean \pm Standard Deviation) in Patients with Psoriasis and Controls

	MDA (nmol/ml)	SOD (U/ml)	AOP (nmol-1/ml \times h)
Patients (n=35)	0.047 ± 0.029	5.04 ± 0.69	0.0199 ± 0.0112
Controls (n=24)	0.027 ± 0.019	4.54 ± 0.76	0.0372 ± 0.0182
<i>p</i>	0.005	0.012	0.001

may result in increased lipid peroxidation. In cell membranes, this process may lead to cell damage, by continuing in chain reaction. It is also responsible for phospholipase A2 activation, production of many mediators by arachidonic acid, and deactivation of adenylyl cyclase and activation of guanylyl cyclase leading to a decrease in the cAMP/cGMP ratio responsible for epidermal hyperproliferation.⁵

Increased production of free radicals or ROS may cause oxidative damage on biological molecules, cell membranes and tissues. ROS induced oxidation of polyunsaturated fatty acids in biological systems results in the formation of lipid peroxidation products such as MDA.^{2,8} Higher platelet,¹⁴ erythrocyte,¹⁵⁻¹⁸ tissue,^{16,19} serum,^{20,21} and plasma²² levels of MDA; higher plasma lipoperoxidation products,^{17,23} and a correlation with disease severity^{14,20-23} have been reported in patients with psoriasis previously. However, Yildirim, et al. did not detect any difference in serum MDA levels in psoriatic patients compared to controls.¹⁹ In our study, we detected increased plasma MDA levels in the patients, but no correlation with disease severity as expressed by the PASI score.

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.^{2,9} It has been suggested that increased generation of superoxide anion radicals from neutrophils¹¹ and neutrophil accumulation in psoriatic lesions may cause abundant superoxide production during the phagocytic reaction¹² and systemic activation of circulating neutrophils²⁴ in psoriatic patients. In the present study, we detected a higher plasma SOD activity in patients with psoriasis than controls. Although suppressed SOD activity in erythrocytes,¹⁶⁻²⁰ neutrophils,²⁵ tissue,¹⁶ and plasma¹⁷ have been reported previously, there is only one study showing a higher plasma SOD activity in psoriatic patients¹⁶ in accordance with our study. Therond, et al. had found a higher SOD activity in fibroblasts and erythrocytes of psoriatic patients, which was not correlated with disease severity as expressed by the PASI.²⁶

AOP level provides an overall indication of total enzymatic and nonenzymatic antioxidant

status.^{10,27} Although Severin et al reported that plasma total antioxidant capacity did not differ between psoriasis patients and controls,⁶ decreased total antioxidant activity in plasma,^{17,23,27} and a correlation with worsening of the disease²³ have been reported in previous studies. In our study we also detected decreased AOP in patients with psoriasis compared to controls, although this decrease was not correlated with disease severity.

To our knowledge, our study is the first to show increased ROS levels as reflected by higher plasma MDA levels and SOD activity, and decreased antioxidant activity determined by AOP levels in patients with psoriasis, independent from the severity of the disease as expressed by PASI. We think that increased SOD activity could be caused by increased superoxide anion production during the psoriatic process in the skin as well as activated peripheral neutrophils. Increased superoxide anion production could also induce lipid peroxidation, as reflected by increased MDA levels. As AOP provides an overall indication of enzymatic and nonenzymatic antioxidant status, the decreased AOP levels detected in our study in spite of increased SOD activity may be due to a possible increase in ROS levels other than superoxide anions. In conclusion, our results support the hypothesis that oxidative damage resulting from increased ROS production along with insufficient capacity of antioxidant mechanisms may be involved in the pathogenesis of psoriasis.

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