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Oxidant and antioxidant status in patients with Psoriasis

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ABSTRACT

Psoriasis vulgaris is a chronic inflammatory skin disease characterized by well-demarcated erythema and scaly plaques. The pathogenesis of psoriasis still remains unclear. 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 in not concordant. In this study super oxide dismutase (SOD) enzyme activity, and malon dialdehyde (MDA) and antioxidant potential (AOP) levels in 50 patients with clinically diagnosed psoriasis were investigated and compared with those of 50 age and sex matched healthy control subjects. Clinical severity of the disease was determined according to psoriasis area and severity index (PASI score) in the patients. Our results showed levels of MDA and SOD were significantly increased ($P<0.001$) whereas AOP were significantly decreased ($P<0.001$) in patients with psoriasis as compared to controls. There was no correlation between PASI scores and plasma SOD, MDA and AOP levels. These results provide some evidence regarding the role of increased ROS and decreased antioxidant activity in psoriasis.

Key words : Psoriasis, MDA, SOD, AOP.

Psoriasis is the dermatological disorder characterized by hyperproliferation and inflammation of the skin. The symptoms of the psoriasis are erythema, itching, thickening and scaling of the skin[12].

The exact etiological factor for psoriasis is yet not clearly known but genetic factor, trauma, skin infection, drugs, emotional stress, alcohol and smoking etc. greatly influences the clinical development of psoriasis[12].

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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. Antioxidants attenuate the damaging effects of ROS and can impare 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 protections. However inadequate antioxidant potential or excess ROS production creates a condition known as oxidative stress, contributing to the development of cutaneous diseases and disorders[11,20].

Malondialdehyde (MDA), is a marker of oxidative stress and specific enzymes that limit free-radical formation, superoxide dismutase (SOD) play an important role in the protection of cell membranes against oxidative damage and may be used as indicators of anti-oxidative status.

It has been suggested that increased ROS production and deficient function of antioxidant systems activities may be involved in the pathogenesis of disease[11,15,18,20]. 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 potentials (AOP) levels and to look for a correlation between their levels and the severity of the disease.

The study was carried out at the Biochemistry & Dermatology Department of large hospital (GMC Bhopal) from Sept 2012 to Jan 2013. Fifty patients of psoriasis with mean age of 41.14±14.25 and without any history of drug therapy for last two months were included in the study. The patients were diagnosed by Auspitz sign, clinical features of psoriasis like erythema, itching, thickening and scaling of the skin and histopathological examination whenever required.

50 age and sex matched normal healthy controls with the mean age of 45±11.62 were selected as controls. The subjects with past or present history of any disease like atherosclerosis, CHD, Diabetes Mellitus etc. which are affecting oxidative stress were excluded from the study.

Out of 50 patients of psoriasis, 42 had plaque type, 5 had guttate type and 3 had palmoplantary type psoriasis. Disease duration ranged from 1 month to 30 years. All patients and control subjects were examined for plasma SOD activity, and MDA & AOP levels. The fasting blood samples for both the groups were drawn into citrate (3.5mg/ml blood) containing glass tubes and centrifuged at 480xg for 10 minutes, and plasma samples were stored at -20ºC until analysis.

Serum malondialdehyde estimation :

This method was based on the fact that lipid peroxide condenses with 1 methyl-2 phenyl indole (MPI) under acidic conditions resulting in the formation of a red chromophore. To determine specifically lipid peroxide in

plasma, proteins are precipitated to remove water-soluble MPI reactive substance. The level of lipid peroxide is ex-pressed in terms of malondialdehyde, which is unstable. Tetramethoxypropane, which is converted quantitatively to MDA in the reaction procedure is used as standard. Results are expressed as nmol/ml.

Antioxidant superoxide dismutase assay :

Assay was done by enzymatic kit method. The principle employs xanthine and xanthine oxidase (XOD) to generate superoxide radicals which react with 2-(4-iodophenyl)-3-(4- nitrophenol)-5-phenyltetrazolium chloride to form a red formazan dye. The final results were obtained in the unit of U/gm Hb values. These values were obtained by the first multiplying the test results by 500, that was the dilution constant, and then dividing the new result by haemoglobin numbers.

Plasma AOP level estimation :

Plasma AOP level estimation is 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 $nmol^{-1}$/ml x h. All procedures were performed at ±4 ºC through the experiment.

Statistical analysis was done using t test. Correlation between the variables was estimated by Pearson's Correlation coefficients.

In the patient group, the mean disease duration was 7.94±8.23 years (range 1 month to 30 years). The results of the plasma levels of MDA, SOD and AOP in patients and controls are summarized in table 1.

Table 1. Plasma Malondialdehyde (MDA), Superoxide Dismutase(SOD) and antioxidant potential (AOP) levels (mean ± standard deviation) in patients with psoriasis patients and controls

	MDA (nmol/ml)	**SOD (U/gm Hb)**	**AOP ($nmol^{-1}$/ml x h)**
	Mean ± SD	*Mean ± SD*	*Mean ± SD*
Patients (n=50)	1.74±0.26	5.39±0.39	0.0196±0.0122
Controls (n=50)	0.91±0.22	4.22±0.48	0.0364±0.0188
P Value	0.001	0.001	0.001

Table 1 depicts the levels of MDA and SOD were significantly increased (P<0.001) in psoriatic patients as compared to normal healthy controls. The level of AOP antioxidant were significantly decreased (P<0.001) in psoriatic patients as compared to controls.

Psoriasis is a chronic inflammatory

skin disease characterized by pathological skin lesions due to various exogenous and endogenous factors and is associated with a number of biochemical and immunological disturbances.

Psoriasis is considered to be an (auto) immune disorder, probably initiated by the overactive skin innate immune system, and maintained by immigrating activated type 1 T cells and abnormally proliferating and differentiating keratinocytes. A complex network of cytokines and chemokines mediates the pathological reaction, whereas the abnormal function of psoriatic regulatory T cells is likely responsible for the chronic nature of psoriasis[8].

Increased production of free radicals may cause oxidative damage on biological biomolecules, cell membranes and tissues. The free radicals induced oxidation of polyunsaturated fatty acids results in the formation of lipid per-oxidation products such as MDA. Our study indicates an increase in the level of MDA (Table 1) in psoriatic patients as compared to normal controls, which is in correlation with the studies of Rocha Pereira P. *et al.*[17] and Relhan V *et al.*[16]. However, Yildrium *et al.*[24] did not find any correlation in the levels of MDA in patients of psoriasis with that of controls.

Increased concentration of the oxidants and decreased concentration of antioxidants leads to oxidative stress, which indicates lipid peroxidation. This may lead to cell damage by continuous chain reactions. In addition, it may be responsible for activation of phospholipase A2, production of many mediators by arachidonate, deactivation of adenylate cyclase and activation of guanilate cyclase leading to decrease in the cAMP/cGMP ratio responsible for epidermal proliferation[15,23].

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[5,11]. It has been suggested that increased generation of superoxide anion radicals from neutrophil[13] and neutrophil accumulation in psoriatic leisions which may cause abundant superoxide production during the phagocytic reaction[21] and systemic activation of circulating neutrophil[9] 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[4,22,24], neutrophil[3], tissue[22] and plasma have been reported previously, there is only few studies like Utas[22] and Baz *et al.*[2] and Therond *et al.*[19] which shows a higher plasma SOD activity in psoriatic patients[22] in accordance with our study.

AOP level provides an overall indication of total enzymatic and non enzymatic antioxidant status[6,14]. Although Severin et al reported that plasma total antioxidant capacity did not differ between psoriasis patients and controls[18], decreased total antioxidant activity in plasma[6,17], and a correlation with worsening of the disease[17] 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 shows 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 non-enzymatic antioxidant status, the decreased AOP levels detected in our study inspite 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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