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Original article:

Plasma oxidant / antioxidant status in psoriasis patients with arthritis

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ABSTRACT

Psoriasis patients often suffer from arthritis. Psoriasis is associated with elevated free radical levels and low antioxidants. Researchers have found variable results with regard to the levels of free radicals and antioxidants. We assayed plasma levels of the free radical marker malondialdehyde (MDA) and the antioxidant superoxide dismutase (SOD) in 83 patients and 69 control subjects. Plasma malondialdehyde levels were highly significantly raised and superoxide dismutase levels significantly raised in the patients when compared to controls. These results might aid further research work in determining the balance between oxidants and antioxidants in psoriasis patients with arthritis and help to plan management of patients.

INTRODUCTION

Psoriasis is a multisystem disease with predominantly skin and joint manifestations affecting approximately 2% of the population (1). The skin is a major target of oxidative injury due to reactive oxygen species which are derived from the environment and also from skin. oxidative stress is caused by a relative overload of oxidants, i.e., reactive oxygen species. This impairs cellular functions and contributes to the pathophysiology of many diseases , for example arthritis. . To protect cells from the damage caused by free radicals and related reactants, organisms have evolved several defense mechanisms to rapidly and efficiently remove ROS from the intracellular environment (2) . When the equilibrium between free radicals (oxidants) and antioxidant defense systems is imbalanced in favor of oxidants, the condition causes what is known as oxidative stress (3). The oxidants that are not directly scavenged or otherwise not metabolized attack cellular components producing useless molecular debris and sometimes cell death. Though many researchers have investigated oxidants and antioxidants in psoriatic arthritis (PA), a definitive conclusion is yet to be reached (5,6). So, we tried to assess the relative roles of oxidants and antioxidants in PA by measuring their respective markers, MDA and SOD.

MATERIALS AND METHODS

The present study was undertaken in a tertiary care hospital. The duration of the study was 14 months. The cases comprised of 83 patients with PA who were selected randomly from the outpatient department . 69 age and sex-matched patients with psoriasis but without any evidence of arthritis were selected as controls Complete history and physical examination of all cases and controls were undertaken, None of the subjects had any history of

systemic or topical drug treatment for one month prior to the study. The subjects did not suffer from any other disease. There was no difference in the parients and controls with respect to smoking or alcohol habits. The study was approved by the local ethical committee and all patients and control subjects gave their informed consent to take part in this investigation.

Venous blood sample was collected from each case and control after 12 hours of fasting. All samples were coded and assayed in a blind fashion by an investigator who was unaware of the subjects' clinical status. Plasma SOD levels were assayed in all subjects (7) . Plasma MDA levels were assayed in all subjects by TBARS method (8).

Statistical analysis of the data was performed by using Statistical Package for Social Sciences (SPSS version 20) and inferences were drawn. $P < 0.05$ was considered to be significant.

RESULTS:

The patients included 43 males and 40 females, aged 43-58 years with a mean age of 49 years and mean duration of disease 17 years. Controls included 37 males and 32 females with a mean age of 47 years and mean duration of disease 19 years.

Table 1. SOD and MDA levels (mean± Standard deviation) in patients and controls

	SOD(U/ml)	MDA(nmol/ml)
Controls (n=69)	6.3 ± 1.1	0.046+ 0.009
Patients (n=83)	5.9 ± 0.9	0.054+ 0.012

Unpaired *t* test results for SOD

P value and statistical significance:

The two-tailed P value equals 0.0148

By conventional criteria, this difference is considered to be statistically significant.

Confidence interval:

The mean of Group One minus Group Two equals -0.400

95% confidence interval of this difference: From -0.721 to -0.079

Intermediate values used in calculations:

t = 2.4660

df = 150

standard error of difference = 0.162

SOD levels in the patients were significantly decreased with respect to the controls.

Unpaired t test results for MDA

P value and statistical significance:

The two-tailed P value is less than 0.0001

By conventional criteria, this difference is considered to be extremely statistically significant.

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Confidence interval:

The mean of Group One minus Group Two equals 0.00800

95% confidence interval of this difference: From 0.00454 to 0.01146

Intermediate values used in calculations:

t = 4.5704

df = 150

standard error of difference = 0.002

DA levels in the patients were highly significantly increased with respect to the controls.

DISCUSSION

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 (9). In very early phase of developing psoriasis lesions, macrophages were seen within the epidermis followed by lymphocytes. During subsequent development neutrophils began to appear between the upper layers forming pockets (10).

The infiltrated and activated leukocytes might lead to release ROS via processes like respiratory bust. Polymorphonuclear (PMN) leukocytes have the potential to damage surrounding tissue by releasing superoxide anion radical produced via NADPH oxidase/myeloperoxidase (11). Superoxide is an important oxygen-derived free radical species (12). Hydrogen peroxide is also produced, though in small quantities, in human body, as a result of various physiological processes. Hydroxyl free radical is another radical which can cause much harm to the tissues. Numerous other free radical species are produced and cause damage to cells, leading to inflammation and other pathological processes (13). The free radicals are highly reactive and extremely short-lived with half-lives of fractions of seconds. So, direct measurement of free radicals is practically not feasible. Thus, conventionally, indirect markers of free radical-mediated tissue damage products like MDA, TBARS, allantoin, etc are commonly assayed. The determination of MDA has attracted widespread interest, because it appears to offer a facile means of assessing lipid peroxidation (14). MDA is one of the final products of polyunsaturated fatty acids peroxidation in the cells. An increase in free radicals causes overproduction of MDA. MDA level is commonly known as a reliable marker of oxidative stress (15).

Humans have evolved to defend themselves against active oxygen species with a complicated defense mechanism; these defenders are known as antioxidants (16). Various enzymes and compounds protect the cell against free radicals - examples include SOD.,catalase, glutathione peroxidase, the vitamins C,E ,carotenoids, etc. All these together provide a solid support to the cell by preventing oxygen into transforming to free radicals. Studies in this field of action and role of antioxidant enzymes in psoriasis have varying results because SOD cativity is assayed in different tissues (RBC, skin, fibroblasts, etc).

In our study we found that SOD levels in the patients were highly significantly decreased with respect to the controls. Though it is difficult to unequivocally establish the cause of this lowering of SOD levels, this decrease might be due depletion of SOD by increased levels of superoxide , which are produced in various tissues like RBC, fibroblasts, neutrophils, etc. Our study also found highly significantly increased MDA levels in patients with respect to the controls. Higher platelet , RBC(17), tissue(18) levels of MDA in psoriasis, compared to normal healthy

individuals, have been reported by various workers. Increased nitric oxide levels are present in serum in psoriatic patients (19). Increased superoxide generation by normal granulocytes has been found in sera from patients with psoriasis (20). Probably, increased superoxide levels cause higher levels of MDA, which is reflected in our study also. To our knowledge, our study is the first to demonstrate high ROS levels , reflected by high MDA levels, as well as low antioxidant levels, showed by low SOD levels, in psoriatic arthritis. As free radical-induced damage is thought to be one of the important factors in the etiopathogenesis of PA, in our opinion, treatment guidelines should include optimal strengthening of antioxidant defense.

This study has limitations that must be considered. To assess free radical –induced damage, the TBARS method was used. MDA can be estimated by various methods, but the present method was employed as it is the most commonly used, time tested and standard method. Also, number of patients in the study groups was not large. Thus, care must be taken in extrapolating the present findings to other populations. Still, we think that our study points towards using MDA and SOD as important, promising markers for PA. So, further research in this line should be directed to find and confirm definitive association between the balance between oxidants and antioxidants in PA.

CONCLUSION

There is highly significantly raised MDA levels and significantly raised SOD levels in PA. These results might aid further research work in determining the balance between oxidants and antioxidants in psoriasis patients with arthritis and help to plan management of patients.

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