Original article:

Superoxide dismutase and malondialdehyde levels in psoriatic arthritis

Goutam Chakraborti[1] , *Rabindranath Biswas[2]

[1] Associate Professor, Department of Biochemistry, Murshidabad Medical College and Hospital, Berhampore, West Bengal, India

[2] Corresponding author , Assistant Professor, Department of Dermatology, Murshidabad Medical College and Hospital, Berhampore, West Bengal, India

Corresponding author*

Abstract

Psoriatic arthritis (PA) is a common sequelae of psoriasis. Increased free radical production and resultant decrease of antioxidants occur in psoriasis. Several workers have studied the oxidant/antioxidant status in PA, but the results are not conclusive. Superoxide dismutase (SOD) and malondialdehyde (MDA) levels in 54 patients with PA were compared to those of 43 controls. Plasma SOD levels were found to be significantly lower in patients with respect to those of controls. Also plasma MDA levels were found to be significantly higher in patients than those of controls This study may help to point at the role of free radicals and antioxidants in the pathophysiology of PA.

Introduction

Psoriasis, a common skin disease, often leads to PA, which is an inflammatory joint disease distinct from other chronic arthritides(1). The skin is susceptible to injury from free radicals, derived from the environment and other sources. Increased free radical production and resultant decrease of antioxidants occur in psoriasis(2). Various free radicals like hydroxyl, peroxyl,superoxide,hydrogen peroxide,singlet oxygen, etc are produced. These harm the different tissues of the body. The free radicals , in turn, are destroyed, partly or fully by antioxidants. Thus antioxidants try to restore the healthy balance disrupted by the harmful radicals. But if antioxidants are overpowered by free radicals, tissue damage can occur and lead to destruction of various tissues like joints leading to arthritis.

The role of free radicals in PA have been studied by different groups but a concrete decision is yet to be reached (3,4,5,6). There is paucity of data available in the literature regarding serum SOD and MDA levels in PA patients, particularly from our country. There are conflicting reports of association of SOD and MDA levels among PA patients. In this study the levels of SOD and MDA have been measured in a decisive attempt to evaluate the role of antioxidants and free radicals in PA.

Materials and methods

This case-control study was conducted for 6 months in a tertiary care hospital in eastern India. 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. 54 patients with PA who were selected randomly from the outpatient department . 43 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. Five milliliter of 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 :

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

	SOD(U/ml)	MDA(nmol/ml)
Controls (n=43)	6.7 + 0.78	0.042+ 0.013
Patients (n=54)	5.1 + 0.69	0.051+ 0.009

The patients included 30 males and 24 females, aged 41-59 years with a mean age of 47 years and mean duration of disease 19 years. Controls included 22 males and 21 females with a mean age of 46 years and mean duration of disease 21 years.

The levels of SOD in both the groups are summarized in Table 1.

Confidence-interval:

The mean of Group One minus Group Two equals 0.7000

95% confidence interval of this difference: From 0.4033 to 0.9967

Standard error of difference = 0.149

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

Unpaired t test results for MDA -

P-value-and-statistical-significance: The-two-tailed-p-value-equals-0.0001

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

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Confidence-interval:

The-mean-of-Group-One-minus-Group

95%confidence-interval of this difference: From -0.01344 to -0.00456

Intermediate-values-used-in-calculations:

t=4.0213

df=95

Standard error of difference = 0.002

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

Discussion

In psoriasis there are alterations in the normal cycle of epidermal development causing epidermal hyperproliferation and vascular changes and inflammation (9).

Various free radicals are highly increased in psoriasis and these cause a number of derangements (10). In normal health, minute amount of oxygen does not undergo complete reduction in the mitochondria, leading to production of free radicals (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

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

individuals, have been reported by various workers. 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. Despite these limitations, we believe that our study points towards using MDA and SOD as important, promising markers for PA. As our findings point to a decrease in the antioxidant SOD, the problem of oxidative stress in PA should also be further investigated in a larger number of patients, and other markers of oxidative stress and antioxidants should be assessed.

Conclusion

To conclude, the results of our study suggest that PA is associated with decrease of SOD levels and increase of MDA levels in serum. SOD and MDA may be potential, useful biomarkers of free radical and antioxidant status in PA for elaboration of treatment strategy and monitoring.

References

1. Common variants at TRAF3IP2 are associated with susceptibility to psoriatic arthritis and psoriasis. Hüffmeier U, Uebe S. Nature Genetics 2010;vol 42, pp 996–999 .

2. The role of oxidants and antioxidants in psoriasis. Yildirim M. Jr Eur Acad Der 2003, Vol17, Issue1 pp 34-36

3. Smoking and pathogenesis of psoriasis: a review of oxidative, inflammatory and genetic mechanisms. Armstrong A.W., Armstrong E.J., Fuller E.N, Sockolov M.E., Voyles S.V. Br Jr Der 2011,Vol 165, Issue6 pp 1162-1168

4. Interaction(s) between essential fatty acids, eicosanoids, cytokines, growth factors and free radicals: Relevance to new therapeutic strategies in rheumatoid arthritis and other collagen vascular diseases. Das U.N. Prostaglandins, Leukotrienes and Essential Fatty Acids 1991, Vol 44, Issue 4, pp 201-210

5. Intracellular free radical production in synovial T lymphocytes from patients with rheumatoid arthritis Remans P. H. J., van Oosterhout M. , Smeets T. J. M., Sanders M., Frederiks W. M., Reedquist K. A. Arthritis and rheumatology 2005,Vol 52, Issue7 pp 2003-2009

6. Raised levels of F_2-isoprostanes and prostaglandin $F_{2\alpha}$ in different rheumatic diseases. Basua S, Whiteman M , Mattey D, Halliwell B Annals of the Rheumatic Diseases 2001,Vol 60, Issue 6

7. An assay for superoxide dismutase in mammalian tissue homogenates. Spitz DR, Oberley LW. Anal Biochem. 1989;179:8–18

8. Aldehyde reactivity with 2-thiobarbituric acid and TBARS in freeze-dried beef during accelerated storage. Sun Q, Faustman C, Senecal A, Wilkinson AL, and Furr H Meat Science, 2001,vol. 57, no. 1, pp. 55–60,.

9. Pathophysiology and treatment of psoriasis. Peters BP, Weissman FG , Gill MA
Am JR Health-System Pharmacy 2000, 57(7):645-59

10. Antioxidants and lipid peroxidation status in the blood of patients with psoriasis
Kökçam[a] I, Nazıroğlu M. Clinica Chimica Acta 1999, Vol 289, Issues 1–2, pp 23-31

11. Superoxide dismutase. Fridovich I .Adv Enzymol, 1974; 41: 35-97

12. The biology of oxygen radicals. Fridovich I .Sci Wish DC, 1978; 201: 875-880

13. Biology of disease: free radicals and tissue injury. Laboratory Investigation; a Journal of Technical Methods and Pathology .Freeman BA , Crapo JD. 1982, 47(5):412-426]

14. Methods in Enzymology 1990, Volume 186, pp 421-431 Malondialdehyde determination as index of lipid Peroxidation Draper H.H. , Hadley M.

15. Malondialdehyde (MDA) as a lipid peroxidation marker .Gaweł S , Wardas M , Niedworok E , Wardas ,P. Wiadomosci Lekarskie (Warsaw, Poland : 1960); 2004, 57(9-10):453-455

16. Free radicals, melatonin, and cellular antioxidative defence mechanisms. Reiter RJ: Path Immun Neuroen. docrin Comm Cir,1994; 35: 135-160

17. Effect of fish oil supplementation on erythrocyte lipid pattern, malondialdehyde production and glutathione-peroxidase activity in psoriasis. Corrocher R,[1]Ferrari S, et al[a]
Clinica Chimica Acta 1989, Vol 179, Issue 2, pp 121-131

18. A comprehensive review of biomarkers in psoriasis Rashmi R, Rao K. S. J., Basavaraj K. H. Clin Exp Dermatol 2009. Vol 34, Issue6 ,pp 658-663 .