Int J Pharm Bio Sci 2013 July; 4(3): (B) 1039 - 1044

Research Article **BioChemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

POTENTIAL ROLE OF OXIDATIVE STRESS AND ANTIOXIDANT DEFICIENCY IN PATHOGENESIS OF PSORIASIS

Dr.T.VIVIAN SAMUEL[*1] AND Dr.KRISHNA MURARI[2]

*[*1]Professor, Department of Biochemistry, JJM Medical College, Davangere, Karnataka (INDIA)*
[2] Departmentof Biochemistry, JJM Medical College, Davangere, Karnataka (INDIA)

ABSTRACT

Psoriasis is a common, chronic, inflammatory dermatological disorder with unknown aetiology.Alteration in concentrationof oxidants and antioxidants in serum lead to imbalance known as oxidative stress. This oxidative stress produces some biochemical and inflammatory changes in skin and is suggested as one of the etiopathological factor in development of psoriasis. The aim of our study was to evaluatethe levels of serum oxidants e.g. malondialdehyde and nitric oxide; and antioxidants e.g. superoxide dismutase and total antioxidant statusand correlation of these levels with severity of disease.In our research work we took 60 clinically diagnosed cases of psoriasis and 60 age and sex matched healthy controls.Our results showed increased concentration of oxidants: malondialdehyde, nitric oxide; and decreased concentration in antioxidants: superoxide dismutase,total antioxidant status in serum of psoriasis patients. Observations of our research work provide some evidence regarding the role of oxidative stress and antioxidant deficiency in pathogenesis of psoriasis.

KEY WORDS: Psoriasis, oxidative stress, oxidants, antioxidants

Dr.T.VIVIAN SAMUEL
Professor, Departmentof Biochemistry, JJM Medical College, Davangere, Karnataka (INDIA)

Corresponding author

INTRODUCTION

Psoriasis is a common chronic, inflammatory and proliferative disease of skin. Most characteristic skin lesions are red, scaly, sharply demarcated, indurated plaques presenting particularly over extensor surface and scalp.[1] Skin is a major site of oxidative stress due to production of reactive oxygen species (ROS) in keratinocytes.ROS are generated during normal cellular metabolism and are integral part of cellular functions.[2]Most important ROS are superoxide anions, hydroxyl ions,hydroperoxi radicals and hydrogen peroxide. ROS mediated oxidative injury lead to some important biochemical changes in keratinocytes,e.g. lipid peroxidation, DNA modification and release of inflammatory cytokines.[3]The free radicals induce oxidation of polyunsaturated fatty acids resulting in formation of lipid peroxidation product such asmalondialdehyde (MDA) in plasma membrane of skin cells of psoriatic lesions.[4,5]Keratinocytes of epidermis constitutively express the neuronal isoform of nitric oxide synthase (NOS 1) enzyme. This NOS1 enzyme,following ultra violet radiation releases nitric oxide(NO) in keratinocytes of psoriatic lesions.[6] Nitric oxide itself is a free radical that contains oxygen. Nitric oxide is a double edged sword; on one hand it is essential for life and on the another hand it is toxic.[6,7]Superoxide dismutase (SOD), glutathione peroxidase and catalase are chief constituents of antioxidant defence mechanism in cells. SOD is a powerful antioxidant and protects the cell by scavenging reactive oxygen species.[8]Antioxidant enzyme system present in plasma is principal component of Total Antioxidant Status (TAS). These enzymes are superoxide dismutase, catalase, glutathione peroxidase, glutathionereductase, ceruloplasmin, and proteins such as metallothionein. Deficiencies in any of these enzyme systems leads to decrease in TASof an individual.[8,9]As the part of antioxidant defence mechanism the levels of serum SOD and TAS decrease in the scavenging process of reactive oxygen species in psoriasis patients. Simultaneously if there is an inadequate antioxidant protection or increased ROS generation, it causes an imbalance. This condition is known as oxidative stress. This oxidative stress and antioxidant deficiency play an important role in pathogenesis of psoriasis.[9,10]Hence, this study was carried out to evaluate the oxidative stress and antioxidant deficiency in patients of psoriasis by estimating the serum levels of malondialdehyde, nitric oxide, superoxide dismutase and total antioxidant status. We also observed the correlation between these levels and the severity of the psoriasis.

MATERIALS AND METHODS

The study was conducted from July 2012 to January 2013 in the department of Biochemistry, JJM Medical College; Davangere (Karnataka) on 60 clinically diagnosed cases of psoriasis from department of Dermatology, JJMMedical College and on 60 age and sex matchedhealthy controls taken from general population of Davangere. Prior to study, written consents were taken from psoriasis patients as well as healthy controls. An approval from ethical committee, JJM Medical College, Davangere was also taken before study.The cases were divided into three categories mild, moderate & severe (20 cases in each category) depending upon Psoriasis Area Severity Index (PASI) Score. The subjects with a history of chronic alcohol abuse, diabetes mellitus, cardiovascular disease and any other inflammatory disorders like rheumatoid arthritis, asthma and atopic dermatitis were excluded from study. Patients also taking systemic or topical medication and any phototherapy for at least two months were also excluded from study.Under aseptic precaution 5 ml of fasting blood sample was collected in plane bulb and serum was separated after clot retraction.The level of serum MDA was estimated by Nadiger et al method using spectrophotometer. Level of Serum NO was estimated by Kinetic Cadmium reduction method. Serum SOD activity was measured by Marklund and Marklund method whereas the level of serum TAS was estimated by applying Randox TAS kit component with Trolax as an equivalent standard (Rice-Evans and Miller, 1994) using automatic chemical analyser.The

statistical analysis was performed using SPSS version 16. In this study to evaluate the difference between the cases and control, we used student's t test. Multiple group comparison was done by one way ANNOVA. Results were expressed as mean±SD.A p-value of 0.05 or less was considered as statistically significant.

RESULTS

A total of 60 psoriasis patients with mean age of 40±15 yearscomprising 20 cases in mild, moderate & severe categories each and 60 controls with mean age of 40±15years were investigated in this study.Present study shows that, the levels of serum MDA were significantly increased in mild ($p<0.001$),moderate ($p<0.001$) and severe ($p<0.001$) psoriasis patients as compared to healthy controls (Table1).Furthermore, we found that increase in levels of serum MDA in moderate patients of psoriasis was significantly ($p<0.001$) greater than in mild cases. It was further significantly greater ($p<0.001$)in severe patients as compared to moderate.The degree of increasing levels of serum MDAin mild, moderate and severe cases of psoriasis showed positive co-relation with the severity of psoriasis.In the present study there was statistically significant increased levels of serum NO in mild ($p<0.001$), moderate ($p<0.001$) and severe ($p<0.001$) psoriasis patients as compared to healthy controls(Table 1).Furthermore, we found that increase in serum levels of NO in moderate patients of psoriasis was significantly ($p<0.001$) greater than in mild cases. It was further significantly greater ($p<0.001$) in severe patients as compared to moderate. Increased serum NO levels in mild moderate and severe cases of psoriasis showed positive co-relation with the severity of psoriasis.In the present study we observed that there was statistically significant decreased serum SOD activity in mild ($p<0.001$), moderate ($p<0.001$) and severe ($p<0.001$) psoriasis patients as compared to healthy controls (Table 1). We also found that serum activity of SODin moderate psoriasis patient were significantly lower ($p<0.001$) than the mild, whereas severe psoriasis patients showed significantly greater decrease ($p<0.001$) serum SOD activity as compared to moderate. Severity of psoriasis is negatively co-related with serum SOD activity.In this study we observed that there was statistically significant decreased levels of serum TAS in mild ($p<0.001$), moderate ($p<0.001$) and severe ($p<0.001$) psoriasis patients as compared to healthy controls (Tables 1). We also found that serum levels of TAS in moderate psoriasis patients were significantly lower ($p<0.001$) than the mild, whereas severe cases showed significantly ($p<0.001$) greater decrease in serum TAS levels as compared to moderate cases. Here again, severity of psoriasis is negatively co-related with serum TAS levels.

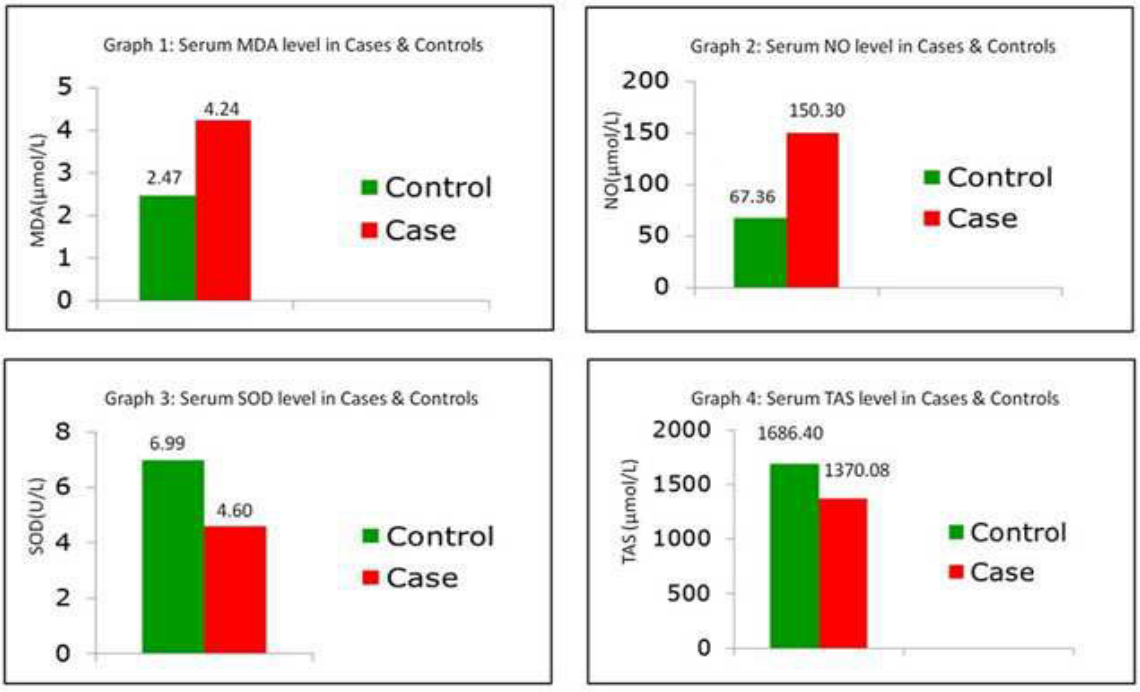
Table-1
Showing the levels of serum MDA, NO, SOD & TAS in controls And psoriasis patients according to category wise.

Parameters	Controls	Mild	Moderate	Severe	P value	F value
Number of Subjects	60	20	20	20		
MDA (µmol/L)	2.47±0.11	3.03±0.25	3.83±0.15	5.88±0.10	0.001	54.7
NO (µmol/L)	67.36±3.49	95.26±5.01	152.10±5.96	203.76±4.06	0.001	17.8
SOD (U/L)	6.99±0.15	5.97±0.10	4.62±0.15	3.43±0.08	0.001	46.1
TAS (µmol/L)	1686.40±30.88	1556.10±13.05	1451.40±13.48	1105.40±18.1	0.001	70.5

Table-2
Showing the cumulative value of serum MDA, NO, SOD & TAS in controls and psoriasis patients.

Parameters	Controls	Cases	p value
Number of subject	60	60	-
MDA(µmol/L)	2.47	4.24	0.001
NO(µmol/L)	67.30	150.30	0.001
SOD(U/L)	6.99	4.60	0.001
TAS(µmol/L)	1686.40	1370.08	0.001

CUMULATIVE GRAPHICAL REPRESENTATION OF DATA



DISCUSSION

Psoriasis is a common chronic inflammatory skin disease characterised by increased keratinocyte proliferation and abnormal differentiation of keratinocytes.[3]Increased chemotaxis, adhesion and increased ROS production in neutrophils are reported in psoriasis patients.[6]Inflammatory process in psoriasis and insufficient antioxidant mechanism leads to ROS generation, this may result in increased lipid peroxidation.[7,8]Ourstudy indicates an increased level of serum MDA in patients of psoriasis (Table 1) as compared to controls, which is also observed in the study ofMadhur Gupta et al [5] , BazKiyamet et al[12], Rocha-Periera et al.[17]A study by Pujari V M, Suryakar A N, IreddyS[4] indicates that there is an increased production of oxidants and increased consumption of antioxidants leading to imbalance of anti-oxidant defence system.This imbalance is considered as etiopathological factor in development of psoriasis.[5,6,17]An evidence from study of NassiriSoheila et al[9]showed that increased oxidant (MDA) production leads to oxidative stress, that is responsible for pathogenesis of psoriasis.[10,11] In plasma membrane of keratinocytes lipid peroxidation leads to cell damage by continuous chain reaction and activation of phospholipase A_2.[15,16]Expression of inducible NOS is responsible for generation of nitric oxide in keratinocytes. This nitric oxide is an important marker of inflammation.[4,7]NOis a potential regulator of keratinocyte growth and

differentiation and is also a specific multifunctional signalling molecule in the cell membrane. NO is considered as a strong component in pathogenesis of psoriasis.[10,16]In our study NO level is significantly increased in patients of psoriasis as compared to healthy controls.A study by A.D. Ormerod, R. Weller, P. Copeland et al[6] and Barker BS, Fry L et al,[16]also showed increased levels of serum NO in psoriasis, that correlates with our study. We also found a positive correlation with severity of disease and serum NO levels.SOD is an antioxidant enzyme thatcatalyses the dismutation of the toxic superoxide radicals produced during oxidative injury. It has been suggested that increased superoxide anion radicals synthesized in neutrophils, accumulate in psoriatic lesions.[4,10]In our study we found significantly decreased SOD activity in serum of psoriasis patients as compared to controls.[13]SOD activity decreased from mild to moderate and moderate to severe cases of psoriasis as compared to controls. We also found negative correlation with disease severity and SOD activity.Total Antioxidant Status is thesum of enzymatic and non-enzymatic antioxidants present in extracellular fluid.[9]TAS is a biomarker of different pathophysiological conditions e.g. cardiovascular disease, diabetes mellitus, neurological and psychiatric disorders, renal disorders and lung diseases.[9,13] In our study we found that there is significant decrease of TAS in serum ofpsoriasis patientas compared to healthy controls.Our research work is supported by a study of Dipali P. Kadam,Adinath N. Suryakar, Rajesh D.Ankush, ChorasiaKadam[10] andKiyamatBaz, M.Y. BurakCimenet al[12], which showed that serum TAS levels decreased in psoriasis patient.We also found a negative correlation of TAS levels and severity of psoriasis.

CONCLUSION

Our study provides evidence to increased ROS production and decreased antioxidant defence in psoriasis, indicated by increased lipid peroxidation and decreased TAS level as well as SOD activity in serum.Inactivating the effect of free radicals and stabilization of the cell membrane thus preventing new epidermal destruction can be achieved by antioxidant supplementation, which can be used as a therapeutic approach. Increased NO level in serum of psoriasis patient may be a result of immunological and inflammatory changes in keratinocytes of psoriasis patients.We also found the positive correlation between increased MDA and NO levels in serum of psoriasis patients with the severity of psoriasis and the negative correlation between decreased TAS, SOD activity in the serum of psoriasis patients with severity of psoriasis.The exact aetiology of psoriasis is still unknown. Our findings support that oxidative stress and antioxidants deficiency have a potential role in aetio-pathogenesis of psoriasis. Finally, we also feel need of further elucidation in pathogenesis of psoriasis. At last our research work will be helpful in making novel strategies for diagnosis, treatment and prognosis of psoriasis.

REFERENCES

1. Griffith CEM, Barker JNWN. Psoriasis In: Tony Burn, Stephen Breathnach, Neil COX, Christopher Griffiths Rook's test book of dermatology Vol. 1st, 8th edi,UK:Wiley-Blackwell.2010;20.1-20.3.
2. Maccrarsone M, Catnic MV, Iraci S, Melino G, Agro AF. A survey of reactive oxygen species and their role in dermatology: EurAcarddermatolveneral1997; 8:185-202.
3. Trouba KJ, Hamadesh HK, Amin RP, Germolec DR,Oxidative stress and its role in skin disease. Antioxid redox signal 2002;4: 665-72.
4. Pujari VM, Suryakar A.N, Reddy IS:Oxidant and antioxidant status in psoriasis patients. Biomedical research 2010; 21(2):221-223.
5. Gupta M, Charis S, Borkar M, Chandankhede M. Dyslipidaemia and oxidative stress in patients of psoriasis.2011;22(2):221-224.
6. OrmerolAD, R.Weller, P Copeland, N.Benzamin, S.H.Ralstone, P.Grabowksi,

R.Herriot: Detection of nitric oxide and nitric oxide synthase in psoriasis. Arch Dermatol Res1998; 290: 3-8.
7. Michael Lieberman, Allan D. Marks. Oxygen Toxicity and Free Radical Injury In: Marks' Basic Medical Biochemistry: A Clinical Approach 3rd edition, Philadelphia:Wolters Kluwer Lippincott Williams Wilkins.2009; 443-463.
8. Ibrahim K, Mustafa N. Antioxidant and lipid peroxidation status in the blood of patient of psoriasis. ClinicachimicaActa:289(1999)23-31.
9. Kusano C and Ferrari B. Total antioxidant capacity: A biomarker in biomedical and nutritional stadies. Journal of cell and molecule biology 2008; 7(1):1-15.
10. Kadam DP, Suryakar AN, Ankush RO, Kadam CY, DeshpandeKH.Role of oxidative stress in various stages of psoriasis. Indian journal of clinical biochemistry 2010; 25(4):388-392.
11. Jyothi RS, Govindswamy KS, Gurupaddappa K. Psoriasis: An oxidative stress condition. Indian journal of clinical and diagnostic research 2011; 5(2):252-253.
12. KiymetBaz et al. Oxidant and antioxidant status in patient with psoriasis 2003; 44(6):987-990.
13. Olgazanov S, Duric J, Dobutonic B, Isenovic ER. Determination of total antioxidant status as a biochemical parameter in control of workers health Arch BiolSci Belgrade 2009; 61(3):375-382.
14. Nassiri S, Malekzad F, Sarlac M, Saeedi M, Hedayati M, Quisari M. Interplay among antioxidant and oxidant in psoriasis. Iranian Journal of Dermatology 2009; 12:56-59.
15. Shilov VN, Sergienko VI. Oxidative stress in keratinocytes as an aetio-pathogenesis factors of psoriasis. Bulletin of experimental biology and medicine 2000; 129(4): 309-313.
16. Barker BS, Fry L.The immunology of psoriasis.British journal of Dermatology 1992; 126:1-9.
17. Rocha-Pereira P, Santos-Silva Alice, Rebelo I, et al. Dyslipidemia and oxidative stress in mild and in severe psoriasis as a risk for cardiovascular disease. ClinicaChimicaActa 2001; 303:33-39.