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Lipid Peroxidation Product As A Marker Of Oxidative Stress In Psoriasis -A Case Control Study In North Coastal Andhra Pradesh

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Abstract:
Background: *In this study we sought to investigate the relation of oxidative stress to Psoriasis by measuring the levels of lipid peroxidation product Malondialdehyde (MDA) and low density lipoprotein (LDL-C).*
Method: *A total of fifty (50) patients with confirmed diagnosis of Psoriasis before starting treatment were included in the study. Twenty five (25) healthy controls were also included in the study for comparison*
Results : *Malondialdehyde (MDA) levels were higher in patients of Psoriasis with 5.81±0.483 nmol/ml (mean ±SD) and the range of 5.0 -6.9 nmol/ml , when compared to controls with 2.63±0.04 nmol/ml (mean ± SD) and range of 2.1 -4.0 nmol/ml with a statistically significant 'p' value of <0.001. Low density lipoproteins-C (LDL-C)values are also increased in Psoriasis cases with a mean ±SD of 182.7 ±17.2 mg/dl, compared to controls with a mean ±SD of 104.5±15.44 mg/dl with a statistically significant 'p' value of <0.0001.*
Conclusion: *Increased level of Malondialdehyde (MDA) can be used as an important biomarker of oxidative stress in Psoriasis.*
Key Words*: Oxidative stress, Psoriasis, Malondialdehyde, Lipid peroxidation.*

I. Introduction

Skin is the largest organ in the body that protects the body from external threats. In the course of providing their protective function skin cells gets damaged so that they must be replaced .So our body produces new skin cells deep in the dermal matrix .These cells migrate upwards towards the surface as they mature. Some mature skin cells undergo a process called keratinization – the conversion of squamous epithelial cells into keratin or simpler structural proteins. Keratinization eventually leads to cell death leaving a layer of drier, harder organic material (cell bodies). In a normal healthy adult, the normal skin turnover occurs once in every 30-40 days. Psoriasis is a chronic inflammatory skin disease characterized by pathological skin lesions due to various exogenous and endogenous factors[1,2]. It is primarily a disorder of excessive growth and reproduction of skin cells due to a fault in epidermis and it's keratinocytes. Exact cause of disease is not known but may be inherited[2]. Several factors like trauma, infection, drugs, metabolic and endocrine factors may provoke Psoriasis[3,4]. Skin contains a well organized system of both chemical and enzymatic antioxidants which protects the skin cells against oxidative damage[1].

Oxidative stress is the damage to cells caused by oxidation, which causes a large increase in the cellular reduction potential[5,6]. More severe oxidative stress can cause cell death and even moderate oxidation can trigger apoptosis (programmed cell death). Oxidative stress causes destruction of cell by the production of Reactive Oxygen Species (ROS). ROS are chemically reactive molecules containing oxygen[7]. In low levels they will be countered by the cell antioxidants. But in severe levels of oxidative stress causes damage to the cells. The damage causes ATP depletion, leading to uncontrolled apoptotic death.

Lipid peroxidation (auto oxidation) is a chain reaction providing a continuous supply of free radicals that initiates further peroxidation in the lipid rich membrane of lipoproteins by ROS like $OH^{\cdot}$ (Hydroxyl radical) $NO^{\cdot}$[nitric oxide radical] O^{2-}[superoxide radical], $ROO^{\cdot}$[Peroxyl radical] etc resulting in generation of lipid peroxidation products like Malondialdehyde (MDA) [9].

MDA (bis –diethylacetal) $CHO\text{-}CH_2\text{-}CHO$, is a dicarbonyl, with a molecular weight of 72 Daltons, formed as a secondary product of endoperoxide during endogenous biosynthesis of prostaglandins and leukotrienes from arachidonic acid and other PUFA. Increased levels of the lipid peroxidation product, Malondialdehyde (MDA) play a very important role in the pathogenesis of Psoriasis.

In the present study plasma MDA levels are estimated by the method of Keisoth (1978) by colorimetric assay with 2-thiobarbituric acid. Serum LDL levels are also estimated.

II. Materials And Methods

Present study was conducted on fifty (50) outpatients of Psoriasis in the department of Dermatology, King George Hospital, Visakhapatnam, Andhra Pradesh, India. Their age group varied from 20-50 years. 25 (twenty five) healthy controls of the same age group were taken. Inclusion criteria; Patients presenting with symptoms and signs of Psoriasis that confirms the diagnosis before starting treatment are included in this study.

Exclusion criteria: Psoriasis patients on treatment. Psoriasis patients with other systemic disorders that interfere with results and Psoriasis patients with other skin diseases are excluded.

Method: Estimation of serum lipid peroxidation product MDA by colorimetric assay with 2-thiobarbituric acid (TBA)by Keisoth [1978] method.

Principle : MDA present in serum is precipitated with weak trichloroacetic acid and boiled for 30 minutes with 0.67% thiobarbituric acid in 2M sodium sulphate reagent in acidic medium (0.05M H_2SO_4) which results in hydrolysis of C=N bonds of conjugated schiff's base of MDA protein adduct. The liberated MDA couples with TBA to form a pink 1:2 (MDA:TBA) adduct. This chromogen is extracted with n-Butanol on cooling and absorbance measured at 532nm.

Procedure : 5ml of blood is taken in a test tube ,serum is separated by centrifugation. Test done by Keisoth method. MDA optical densities were measured colorimetrically. Values obtained by using standard curve. Normal range: 2.6 -3.8 nmol/ml Serum LDL [low density lipoprotein] levels were estimated by Friedwald calculation after estimation of total cholesterol, triglycerides and HDL-C by colorimetry.

III. Results And Observations

In the present study mean values of Malondialdehyde among cases is 5.81 ± 0.483 nmol/ml(mean±SD) with the range of 5.0 -6.9 nmol/ml and that of controls is 2.63 ± 0.044 nmol/ml (mean±SD) with the range of 2.1 – 4.0 nmol/ml. The increase in serum MDA level among cases is significant with a 'p' value of < 0.001.

Mean value of LDL-C among cases is 182.7 ± 17.2 mg/dl (mean±SD) in comparison with the control group with a mean value of 104.5 mg/dl ± 15.44 mg/dl (mean±SD) and a' p ' value of <0.0001, statistically significant.

IV. Discussion

Fifty (50) patients of Psoriasis were studied for MDA level as a marker of lipid peroxidation. Twenty five (25) healthy controls were taken for comparison. In all cases and controls serum MDA and LDL-C levels are measured by appropriate methods.

Skin contains a well organized system of both chemical and enzymatic antioxidants, which work synergistically and protect the skin cells against oxidative injury by reactive oxygen species (ROS). These antioxidants prevent the production of oxidation products like Malondialdehyde (MDA) which harms the cells. But when oxidative stress overwhelms the antioxidant capacity, the subsequent modification of cellular redox apparatus leads to the generation of degenerative processes like peroxisome proliferators activated receptors, whose natural sources are polyunsaturated fatty acids (PUFA).Their oxidant products have a central role in induction of Psoriasis, that indicates links between free radicals and skin inflammation . In the present study lipid peroxidation product MDA levels are elevated in cases (5.81±0.48 nmol/ml) when compared to controls (2.63 ±0.44 nmol/ml) with a ` p' value of <0.001 which is statistically significant. The values in the present study are in consistent with the study of Kokcami Naziroglu M done in November 1999 with a significant ` p ' value of <0.001 and also with the study of Yonsei Med J done in December 2003 with a significant ` p ' value of <0.005.

Serum LDL-C (Low Density Lipoprotein-C) levels are also increased significantly in cases (mean 182.7± 17.2 mg/dl) compared to controls (mean 104.5± 15.44mg/dl) with a significant ` p ' value of <0.0001. The values in the present study are in consistent with the study of Offidani AM, Ferretti G 1994 with a significant ` p ' value of <0.01 and also with the study of Vanizor Kural B , Orem A, Cimsit G Feb 2003 with a significant ` p ' value of < 0.01. Increased lipid peroxidation causes increased oxidized LDL-C which itself produces inflammation and also produces ROS species. As the increased LDL-C produces plaques, patients of Psoriasis are more prone for atherosclerosis and coronary artery disease (CAD), for which their cardiac status has to be evaluated[10] .

V. Conclusion

From the above study it was evident that Malondialdehyde (MDA) and low density lipoprotein – C (LDL-C) levels are important biomarkers of oxidative stress due to increased lipid peroxidation which is a risk factor for chronic skin disease like Psoriasis.

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