STUDY OF MDA AND SGPT LEVELS IN PATIENTS WITH PSORIASIS

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ABSTRACT

BACKGROUND
Skin is a major target of oxidative stress due to reactive oxygen species (ROS) that originate in the environment and in the skin itself. Psoriasis is a common chronic and recurrent inflammatory skin disorder that has been associated with abnormal plasma lipid metabolism. Psoriasis is considered to be an (auto) immune disorder, probably initiated by the overactive skin innate immune system. Increased production of free radicals may cause oxidative damage on biological bio molecules, 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. Oxidative stress has been implicated as important cause of Methotrexate (MTX) induced liver toxicity.

AIMS
The objective of our present study is to evaluate if psoriasis is associated with oxidative stress and hepatotoxicity.

SETTINGS AND DESIGN
50 patients suffering from psoriasis who have attended the D.V.L O.P. of G.S.L Medical College and general hospitals are taken as cases and compared with 50 healthy controls.

MATERIALS AND METHODS
Venous samples are collected and MDA levels are estimated using TBARS method and SGPT levels using fully automated analyzer.

STATISTICAL ANALYSIS
Statistical analysis is performed using software GraphPad QuickCalcs.

RESULTS
MDA levels in psoriatic patients showed significant increase in their levels compared to control and also there is significant rise in SGPT levels in patients when compared to control group.

CONCLUSION
Increased MDA levels show that there is oxidative stress in psoriatic patients and there is also hepatotoxicity which can be attribute to either oxidative stress or the effect of medications used to treat psoriasis.

KEYWORDS
Psoriasis, MDA, SGPT.


INTRODUCTION
Psoriasis is the most common chronic inflammatory skin disease, affecting about 2% of the general population. 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.[1-2] The skin is potential target organ for oxidative injury because it continuously exposed to visible and ultraviolet irradiations and high oxygen concentration.

The skin is also major organ for the entry of many airborne environmental pollutants; some of them are free radical generating agents.[3]

Since last one decade, the researchers have intensely focused on and proposed the involvement of oxidative stress in psoriasis.

Psoriasis is a chronic inflammatory skin disease which is characterized by an increased prevalence of obesity, hypertension, hyperlipoproteinaemia and oxidative stress, leading to occlusive vascular diseases, cardiovascular accidents, arthritis, diabetes and liver diseases.[4],[5],[6] Several studies have attributed obesity, hypertension and hyperlipoproteinaemia to retinoids, corticosteroids and thiazide diuretics, and liver disease to cyclosporine and methotrexate (Anti-metabolites) which are used in the treatment of psoriasis.[7],[8]

Meta-analysis has revealed the incidence of progression of liver disease (Worsening of 1 grade on the histological classification of Roenigk) in patients with psoriasis averages 27%, or 7% per gram of MTX (Total dose) given. Chronic hepatotoxicity typically develops only after chronic use of higher doses (2 years or more of total doses of 1.5 grams or
more), is more likely in patients who ingest ethanol, who are aged, who are obese, who have chronic renal insufficiency, or who have diabetes.

Methotrexate (MTX), an antimetabolite drug, acts as a dihydrofolic acid analogue that binds to the dihydrofolic acid reductase enzyme by inhibiting the synthesis of tetrahydrofolate, which is required for DNA synthesis.

MTX associated hepatotoxicity is a significant clinical problem that affect the compliance with MTX-containing treatment regimens. The development of MTX-induced liver toxicity is not rare and mainly depends on the duration and the dose of drug. Renal insufficiency, obesity, alcohol consumption, diabetes, and older age are other contributing factors.[9]

There are several studies investigating the role of oxidant/antioxidant systems in the pathogenesis of psoriasis with discordant results.[10,11]

**METHODS**

A case control study, done in the department of Biochemistry, G.S.L. Medical College & General Hospital. Fifty patients of psoriasis with a mean age of 40-50 years were included in the study. Fifty age and sex matched normal healthy controls were selected as controls. The patients were diagnosed by Auspitz sign, clinical features of psoriasis like erythema, itching, thickening and scaling of the skin. The clinical severity was determined according to the Psoriasis Area and Severity Index (PASI) score.

Eligible patients had stable moderate to severe plaque psoriasis for ≥ 6 months, psoriasis involving ≥ 10% of body surface area (BSA), a PASI ≥ 10 at screening and baseline, and were candidates for systemic therapy or phototherapy in the opinion of the investigator. Patients with any chronic inflammatory disease, diabetes mellitus, renal disorders, IHD, hypothyroidism, nephritic syndrome, obstructive liver disease, any other skin disorder were excluded from the study. All the patients who are on beta blockers, thiazides, retinoids, cyclosporine and lipid lowering agents in the recent 6 months were excluded from the study. 5 ml of venous blood samples was collected in a bottle without adding any anticoagulant from patients with psoriasis and normal healthy individuals. Blood samples were centrifuged at 3000g for 10 minutes and were estimated for MDA and SGPT levels.

MDA was estimated by TBARS method, Mahalouz et al. Under acidic conditions, lipid peroxides break down to form MDA which complex with TBA. The resulting MDA – TBA chromogen is measured at 530nm against distilled water in spectrophotometer.

SGPT is estimated by IFCC kinetic method using fully automated analyzer.

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, revised in 2000.

**RESULTS**

The statistical method used to analyze the results is a software GraphPad QuickCalcs. Unpaired t-test was done.

From table 1, it is seen that the mean values of MDA are more in cases (5.28±0.659) when compared to controls (1.21±0.337). Similarly the mean values of SGPT are more in cases (69.10±7.55) compared to control group (20.59±4.50).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cases Mean ± SD</th>
<th>Controls Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA</td>
<td>5.28±0.659</td>
<td>1.21±0.337</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SGPT</td>
<td>69.10±7.56</td>
<td>20.59±4.90</td>
<td>&lt;0.0001</td>
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</tbody>
</table>

**DISCUSSION**

We found in our study that the psoriatic patients had significantly increased MDA and ALT levels as compared to the control subjects, which was in accordance with the findings of other studies.[12,13] Although there have been extensive studies on the roles of serum lipids, oxidants and antioxidant levels in psoriasis, their importance in the aetiology or in the enhancement of the disease remains controversial.

Skin is a major target of oxidative stress due to reactive oxygen species (ROS) that originate in the environment and in the skin itself. ROS generated during normal metabolism, are an integral part of normal cellular function, and are usually of little harm because of intracellular mechanisms that reduce their damaging effects. Antioxidants attenuate the damaging...
effects of ROS and can impair and/or reverse many of the events that contribute to epidermal toxicity and disease.

However, increased or pro-longed free radical action can overwhelm ROS defence mechanisms, contributing to the development of cutaneous diseases and disorders. [14] Although ROS play a role in diseases such as skin cancer, their biological targets and pathogenic mode of action are still not fully under-stood. In addition, strategies useful in the therapeutic management of ROS action in human skin are still lacking.

Increased ROS production in patients of psoriasis, [15] 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 guanylate cyclase leading to decrease in the cAMP/cGMP ratio responsible for epithelial proliferation in patients of psoriasis. [16] Psoriasis is considered to be an (Auto) immune disorder, probably initiated by the overactive skin innate immune system. 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. Increased ROS production in patients of psoriasis, [17] and decreased concentration of antioxidants leads to oxidative stress, which indicates lipid peroxidation. This may lead to cell damage by continuous chain reactions.

In this study we found MTX induces significant impairment in the liver function. SGPT levels were significantly raised. These findings are in agreement with the reports by Suleyman et al., 2008 and Assma. [18,19] Moreover in the present study we demonstrated that MTX treatment causes significant increase in MDA as compared to control. Similar findings were reported by Kaplowitz, 2000 and Suleyman et al., 2008. [20,21] The finding of elevated MDA in our study suggesting the presence of enhanced lipid peroxidation due to MTX treatment.

Chronic treatment with MTX reported to produce fatty liver and hepatic fibrosis and also portal hypertension in some cases. Further, MTX produces hepatic and renal oxidative stress on chronic exposure. [22,23] Administration of MTX for a period of 6 weeks showed increase Thiobarbituric acid reactive substance (TBARS) content and decrease in the activities of superoxide dismutase, catalase, and glutathione reductase in rats. [24]

It is well known that MTX induces oxidative stress by increasing lipid peroxidation in different tissues. [25] The reactive oxygen species (ROS) thus formed from oxidative stress further leads to the cellular damage by peroxidation of membrane lipids, protein cross-linking and DNA breakdown. [26-28] showed that hydrogen peroxide is implicated in MTX induced lipid peroxidation.

Increased liver markers such as SGOT, SGPT and ALP activity was observed in MTX intoxicated rabbit which shows the increased permeability, damage or necrosis of hepatocytes. [29,30] showed that MTX induces apoptosis through oxidative stress pathway.

Oxidative stress has been implicated as important cause of Methotrexate (MTX) induced liver toxicity. Prolonged use of MTX leads to accumulation of polyglutamate forms of the drug in hepatocytes. The presence of higher levels of polyglutamates causes a longer intracellular presence of the drug, and this has been suggested as a mechanism for MTX hepatotoxicity. [31] Recently, hydrogen peroxide molecules were reported to act as mediators both in the therapeutic and toxic effects of MTX. [32] Oxidative stress and lipid peroxidation mediated by oxygen free radicals has been implicated as an important cause of MTX induced liver toxicity. [33] Lipid peroxidation, mediated by oxygen free radicals (ROS), might be an important cause of hepatic damage and alteration in liver function profile. The lipid peroxidation causes disruption of the membrane bilayer and cell integrity and eventually hepatic necrosis that leads to leakage of liver (Cyttoplasmic) enzymes into the blood. [34,35]

The results of earlier studies indicated significant increase in serum levels of MDA, [36-39] as well as positive correlation between increased serum MDA level and the severity of psoriasis. [40,41] There were few studies showing non-significantly increase or unchanged levels of MDA in the serum of psoriasis patients. [42]

Increased lipid peroxidation is indicated by increased concentration of Malondialdehyde (MDA). [43] 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 (Micro-abscesses). Neutrophil migration into the epidermis was most pronounced in active disease and occurred in a rhythmic pattern. [44] The infiltrated and activated leukocytes might lead to release ROS via processes like respiratory burst.

Polymorphonuclear (PMN) leukocytes have the potential to damage surrounding tissue by releasing superoxide anion radical produced via NADPH oxidase/myeloperoxidase which further give rise to other activated oxygen species which all together were known to induce lipid peroxidation. ROS in turn also stimulates PMN recruitment by increasing PMN adhesion to endothelium. [45]

The increased generation of ROS, by increased infiltration and activation of PMNs might target cellular polyunsaturated fatty acids for lipid peroxidation, which might indicate by the increased concentration of MDA in serum of psoriasis patients.

It was also proposed that the drugs used to treat psoriasis might act as antioxidants and decreasing oxidative stress. Nitric oxide was increased in the serum of psoriatic patients and considered as factor for pathogenesis of psoriasis. It was observed that the level of NO was decreased during the treatment of psoriasis by betamethasone (Topical).

Psoriasis risk was significantly decreased by intake carrots, tomatoes and fresh fruit. The consumption of vegetable and fruits may be beneficial in psoriasis due to their high content of various antioxidants such as carotenoids, flavonoids and vitamin C.

Our study does not include role of diet and NO in psoriasis but they only support our opinion of the possibility of involvement of oxidative stress in pathogenesis of psoriasis.

REFERENCES


