Relationship between Paraoxonase and Malondialdehyde as a marker of oxidative stress in patients with psoriasis

Relación entre Paraoxonasa y Malondialdehído como marcador de estrés oxidativo en pacientes con psoriasis

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Abstract

Oxidative stress plays an important pathogenetic role in Psoriasis is a chronic inflammatory, proliferative skin disease characterized by pathological skin lesions due to various exogenous and endogenous factors. Therefore, the aim of the present study was to compare Paraoxonase (PON1), and malindialdehyde (MDA) in patients and in healthy age-matched subjects, taking into account biochemical correlates. The study was carried out in the two age-matched groups of men. Group I consisted of 50 psoriatic patients aged (34.8–77.0) years.

Results: A total of 50 patients (46 women and 74 men) and 40 healthy gender- and age-matched controls were enrolled in the study. Increased lipid peroxidation (MDA) (339.86± 29.97 vs 229.39± 13.85: < .001). as well as downregulated PON activity (0.92± 0.09 vs1.37± 0.29: < .001) were found in psoriatic patients compared with controls. Receiver operator characteristic curve investigation shown the levels of PON and MDA are the best biomarkers differentiating subjects with psoriasis. Furthermore, a significant negative correlation was found between PON and MDA, with a moderate effect size correlation coefficient of -.34 (p =.014, 95 % Confidence interval = [-.57, -.07]). This implies that MDA has a tendency to decrease as PON increases.

Conclusion: This study indicates that serum PON1 together with MDA, is a useful and novel marker for evaluating the disease status and activity of patients with Psorasis.

Keywords: Psoriasis, Oxidative balance, paraoxonase-1, MDA.

Resumen

El estrés oxidativo juega un papel patogénico importante en la psoriasis, que es una enfermedad cutánea inflamatoria y proliferativa crónica caracterizada por lesiones cutáneas patológicas debido a diversos factores exógenos y endógenos. Por lo tanto, el objetivo del presente estudio fue comparar la paraoxonasa (PON1) y el malindialdehído (MDA) en pacientes y en sujetos sanos de la misma edad, teniendo en cuenta los correlatos bioquímicos. El estudio se llevó a cabo en los dos grupos de hombres de la misma edad. El grupo I constaba de 50 pacientes con psoriasis de (34,8–77,0) años de edad.

Resultados: se inscribieron en el estudio un total de 50 pacientes (46 mujeres y 74 hombres) y 40 controles sanos emparejados por sexo y edad. Aumento de la peroxidación lipídica (MDA) (339,86± 29,97 vs 229,39± 13,85: < ,001). Así como una actividad de PON regulada a la baja (0,92± 0,09 frente a 1,37± 0,29: < 0,001) se encontraron en pacientes con psoriasis en comparación con los controles. La investigación de la curva característica del operador del receptor mostró que los niveles de PON y MDA son los mejores biomarcadores que diferencian a los sujetos con psoriasis. Además, se encontró una correlación negativa significativa entre PON y MDA, con un coeficiente de correlación del tamaño del efecto moderado de -0,34 (p = 0,014), 95 % Intervalo de confianza = [-.57, -.07]). Esto implica que la MDA tiene una tendencia a disminuir a medida que aumenta la PON.

Conclusión: este estudio indica que la PON1 sérica junto con la MDA es un marcador útil y novedoso para evaluar

el estado de la enfermedad y la actividad de los pacientes con psoriasis.

Palabras clave: Psoriasis, Balance oxidativo, paraoxonasa-1, MDA.

Introduction

Psoriasis is a chronic autoimmune skin disease, characterized by keratinocyte proliferation, that is characterized by well-defined red plaques with silvery-white scales, which can involve any region of the skin (and other components of the integumentary system, including the nails), but is usually located on the elbows, knees, scalp and presacral region. Psoriasis is estimated to affect approximately 125 million people around the world, psoriasis can start at any age (but often presents between 15 and 30 years) and appears to be equally common in both male and female patients. While in most cases psoriasis is benign, in 10% of cases it can be serious (because of its spread on the body or its complications). Psoriasis appears to reduce lifespan by 3.5-10 years, with early disease onset reducing life expectancy by up to 20 years[1-3].

The most common form is psoriasis vulgaris, also called plaque-type psoriasis, which accounts for ~80% of all psoriasis cases, and has a massive impact on quality of life. Psoriasis is today considered to be a systemic inflammatory disease associated with a higher risk of various concomitant diseases, including cardiovascular diseases, obesity, diabetes mellitus, metabolic syndrome, or psoriatic arthritis (PsA)[4].

Oxidative stress, a pathophysiologic imbalanc induced in the body when the amount of reactive oxygen species (ROS) in cells surpasses the capacity of antioxidant. These are normally produced in cells, playing important roles in cell signaling. However, when produced over the antioxidant capacity of the cell, ROS lead to the disruption of redox signaling and to molecular damage, which can ultimately result in cell death, plays a significant role in the pathogenesis of many diseases and mechanisms of complications[5-9].

Skin exposure to a number of irritants or proinflammatory agents including UVA and UVB generates ROS through the oxidative burst in infiltrating leukocytes at the site of inflammation which damages the skin cells[10].

OS is one of the most important, quite often overlooked points in Ps. This complex, multifactorial syndrome is characterized by the occurrence of inflammatory infiltrates in hyperplasia and abnormally differentiated dermo-epidermal skin. In turn, human skin is a potential target for oxidative injury, as it is continuously exposed to environmental stimuli generating ROS. Several conditions, such as infections, skin traumas, oxidant drugs, and stress factors, may cause and trigger the enhancement of Ps[11].

Paraoxonase (PON1, EC 3.1.8.1)is a 45-kDa glycoprotein ,calcium-dependent enzyme has serum esterase activity in the liver, kidney and small intestine. synthesized in the liver and circulating in the blood attached to high-density lipoproteins (HDL). PON1 protects plasma lipoproteins including low-density lipoproteins (LDL) and HDL themselves from oxidative modification by decomposing lipid peroxidation products such as fatty acid lactones, hydrolyzes multiple bioactive lipid mediators (BLM) including oxidized phospholipids and eicosanoids[12-16].

Aim of this study to assess paraoxonase,and malondialdehyde as amarker of oxidative stress markers in in patients with Psoriasis .

Materials and methods

This is a cross sectional, hospital based study. The protocol of this study was approved by the scientific committee of Tikrit University College of medicine, the agreement of attendance to, Kirkuk general hospital that approved by Kirkuk health directorate, to collect the samples from the patients and Baghdad governorate in Medical City Hospital. This study was carried out from 1st January 2022 to 30th June.

Blood samples were obtained from the patients and control. Blood samples of 5 ml were taken from antecubital vein puncture. The blood sample obtained from each subject was transferred into gel tube for separation of serum. Then blood in the gel tubes were then allowed to clot at room temperature (25 ˚C) for 30 minutes. After that centrifugation was done at (4000) rpm for 10 minutes to separate the serum. The serum of each patient and control was divided and stored in to 3 small tubes and immediately 3 test was done then the rest stored at -80˚C until the time of analysis to avoid thawing and refreezing. Thawing of the samples was allowed to take place at 25˚C before conducting the assay.

Study patients

This study included 90 adult participants divided into two groups:

Case group: Includes 62 patients diagnosed with psoriasis by a Consultant Dermatologist. 30males (60%) and 20 females (40%) with a mean of age of 39.46±14.612 years,

Control group: The control group consists of 40 volunteers, 20 males (50%) and 13 females (50%), with a mean of age of 37.50 ±11.33 years

A detailed medical, general and family history was taken along with a detailed consent form from the study subjects.

Psoriasis patients were further graded according to the Psoriasis Area and Severity Index (PASI)that is usually implemented to measure the condition of skin changes[32].

Statistical analysis

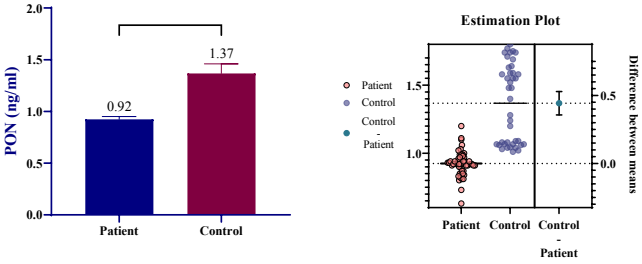
Welch's t-test was used, which has higher statistical power than Student's t-test when the two samples have unequal variances and unequal sample sizes (Ruxton, 2006). Cohen's standard was used to evaluate the strength of the relationships, where coefficients between .10 and .29 represent a small effect size, coefficients between .30 and .49 represent a moderate effect size, and coefficients above .50 indicate a large effect size (Cohen, 1988).

A total of 50 diagnosed cases of aged between to years, and 40 age and sex matched controls were included in the study to assess the role of paraoxonase, and malondialdehyde as amarker of oxidative stress in patients with Psoriasis and healthy individuals

Table 1 Sex frequency and percentages by groups.

	Gender		
group	Female	Male	total
Control	20 (50.0%)	20 (50.0%)	40 (44.4%)
Patient	20 (40.0%)	30 (60.0%)	50 (55.6%)
total	40(44.4%)	50(55.6%)	90
Chi-squared	0.890		
DF	1		
Significance level	P = 0.3455		

Figure 1: Sex distribution according to Psoriasis and healthy individuals



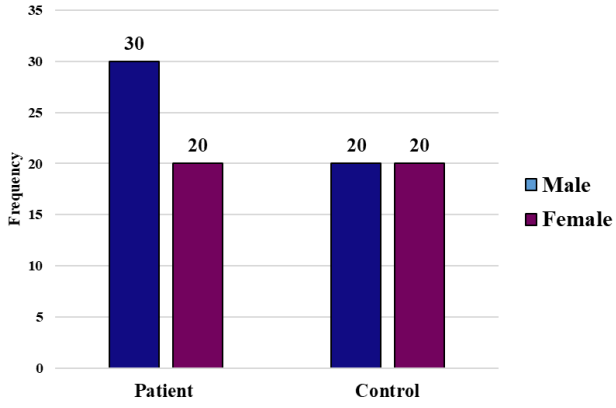
There was not a statistically significant difference between the groups in terms of the genders that were already matched X^2 (1) 0.890 P = 0.3455. out of 50 patients, males made up 60 % of cases, while females made up 40 %. Among the healthy individuals, males and females each made up 50 percent of the sample size. Table 3-1 and (Figure 3-1) include both a frequency and a percentage breakdown of the data.

Table 2: Summary Statistics Table for serum PON and Oxidative stress markers as compared by groups using Two-Tailed Independent Samples t-Test

	Patient	Control			
Variable	M± SD	M± SD	t	p	d
PON	0.92± 0.09	1.37± 0.29	-9.37	< .001	2.08
MDA	339.86± 29.97	229.39± 13.85	23.16	< .001	4.73

The comparison of serum PON, levels of Psoriasis subjects with control group are given in (Table 3-4). Mean serum PON levels were 0.92±0.09 2.18 ng/ml in the study group and 1.37±0.29 ng/ml in the control group (Table-3-4) and the difference was found to be significant t(45.64) = -9.37, p < .001 between both the participating groups. This finding suggests the mean of PON was significantly different between the Patient and Control categories of group. The results are presented in Table 3-5. A bar plot of the means is presented in Figure 3-8 as a bar plot that illustrates the means and the means' estimation difference plot.

Figure 3: Bar plot of mean values with 95% CI error bars accompanied by Estimation plot with 95% Confidence intervals of mean differences between the groups for PON. ** Highly Significant at (p<0.0001).**



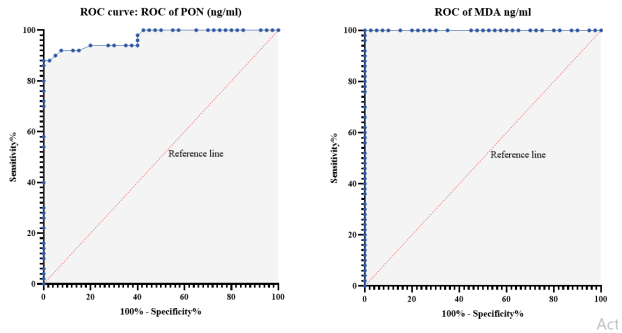
The comparison of the serum MDA levels of patients with psoriasis with those of the control group is presented in (Table 3-4). The control group had mean serum MDA levels of 229.39 (standard deviation = 13.85), while the psoriasis group had mean serum MDA levels of 339.86 (standard deviation = 29.97) (Table-3-4). The difference between the two groups was found to be statistically significant, with t(72.18) = 23.16, p< .001. Based on these findings, it appears that the mean of MDA differed significantly between the Patient category and the Control category of groups.

Receiver operating characteristic curve (ROC) analysis was utilized in order to determine the diagnostic values of PON, MDA, in discriminating the psoriasis patients from control group.

For PON, the area under the curve (AUC) was calculated to be 0.970, the 95 % confidence interval ranged from 0.911 to 0.995, and the level of significance was p < 0.0001. At cutoff values of PON = 1.00, the test had

a sensitivity of 88 % while maintaining a specificity of 100%. whereas in the case of MDA The area under the curve (AUC) was 1.00, with a 95 % confidence interval ranging from 0.960 to 1.000 and the significance level p <0.0001, The sensitivity and specificity were both 100 % at the cutoff for MDA = 260.

Figure 3: scatter plot depicting the correlation between PON and MDA Regression line was added to ease the interpretation



Receiver operating characteristic curve (ROC) analysis was utilized in order to determine the diagnostic values of PON, and MDA in discriminating the psoriasis patients from control group.

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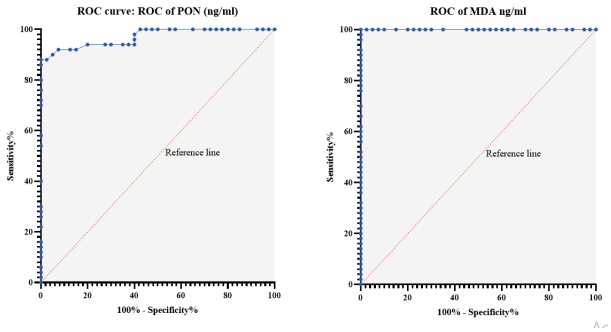
Whereas in the case of MDA. The area under the curve (AUC) was 1.00, with a 95 % confidence interval ranging from 0.960 to 1.000 and the significance level p <0.0001, The sensitivity and specificity were both 100 % at the cutoff for MDA = 260.

Figure 4: ROC analysis for PON (upper left), MDA (upper right), showing area under curve values in context of discrimination between the psoriasis patients from control group.



Discussion

Skin is a major target of oxidative stress because of ROS originating from the environment and skin metabolism. Most important ROS are molecular oxygen (O_2), superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radical (OH), nitric oxide (NO), peroxynitrite (ONOO-) and hypochlorous acid (HOCl). In normal aerobic cells, there is a balance between oxidative damage and antioxidant protections. However, inadequate antioxidant potential or excess ROS production creates a condition known as oxidative stress, contributing to the development of cutaneous diseases and disorders[17].

Plasma membranes of the skin cells in the psoriatic lesion have a significant increase in arachidonic acid, which is the natural substrate for synthesis of malondialdehyde (MDA), an end product of lipid peroxidation and marker of oxidative stress is a reactive aldehyde and is one of the many reactive electrophile species that cause toxic stress in cells[10,18-19].

Our research found a significantly increased level of MDA than the corresponding levels in the healthy control group. The similar findings were documented by previous works[20-21]. Our study provides evidence to increased ROS production, indicated by increased lipid peroxidation 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. These results supported the proposal that serum MDA level could be helpful in predicting the prognosis of psoriasis and add further support for the involvement of oxidative stress in the pathogenesis of psoriasis.

Paraoxonase is one of a family of three enzymes, called PON1, PON2 and PON3, which degrade lipid peroxides in circulating lipoproteins and in the cytoplasmic and intracellular organelle membranes of cells[21]. These enzymes are linked to mitochondria-associated membranes, which modulate mitochondrial metabolism and prevent apoptosis. There are variations of serum PON1 activity in the population[22,23].

Lower PON1 activity was also observed in the sera of psoriasis patients compared with healthy subjects, confirming that psoriasis is associated with OS, and impairment of the antioxidant system in the plasma of patients may play a role in pathogenesis and progression of psoriasis and related complications[12].

Decreased PON-1 activity in psoriatic patients have been attributed to different mechanisms: (a) increased systemic oxidative stress and increased conversion of HDL to a dysfunctional pro-infammatory and pro-atherogenic state[24]. (b) reductions in apolipoproteins in HDL may af-

fect the separation of PON1 from HDL and its subsequent instability, (c) the increase in oxidized lipids caused by oxidative stress may contribute to the inactivation of PON1 (d) increased triglycerides in HDL may affect PON1 activity and (e) increases in blood glucose may reduce PON1 activity through protein glycation, including PON1[25-28].

Result of this study has found PON-1 levels are lower in serum of psoriatic patients when compared with control group confirming that psoriasis is associated with OS, and impairment of the antioxidant system in the plasma of patients may play a role in pathogenesis and progression of psoriasis and related complications. Therefore, the results support previous work by[29-30].

However, other studies have shown negative results. Pektas et al.[31] did not report any change in PON-l activity in psoriatic patients following 30 phototherapy sessions with UVB narrowband lamps. Similarly, Kilic et al.[32], did not observe any increase in PON-l activity in psoriatic patients after 8-week treatment with methotrexate.

Conclusions

The present study indicates that the psoriasis is more susceptible to oxidative damage, suggesting that use of antioxidant therapy may be warranted to ameliorate oxidative stress in this condition. Therefore, the use of exogenous antioxidants may have potential therapeutic benefits in reducing oxidant status in these patients.

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